A Study to Determine the Incidence of Obstetric Cholestasis And to Evaluate Pregnancy Outcome in Women with Obstetric Cholestasis

(A Prospective Study)

DISSERTATION

Submitted To

THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY

For

M.D. DEGREE EXAMINATION

M.D. OBSTETRICS AND GYNAECOLOGY BRANCH – II

KILPAUK MEDICAL COLLEGE & HOSPITAL

CHENNAI – 600 010.

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY

CHENNAI

APRIL – 2013

Certificate

This is to certify that this dissertation titled **"A STUDY TO DETERMINE THE INCIDENCE OF OBSTETRIC CHOLESTASIS AND TO EVALUATE PREGNANCY OUTCOME IN WOMEN WITH OBSTETRIC CHOLESTASIS"** has been prepared by **Dr. E. GEETHANJALI,** under my supervision in the Department of Obstetrics and Gynaecology, Government Kilpauk Medical College, Chennai , during the academic period 2010 – 2013 and is being submitted to the **Tamilnadu Dr. M.G.R. Medical University, Chennai** in the partial fulfilment of the University regulation for the award of the M.D (O & G) and her dissertation is a bonafide work.

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Acknowledgement

I am extremely thankful to **Prof. Dr. A. KALA,** M.D., D.G.O., **Head of Department** for helping me choose this topic and guiding me about the basics of this study.

I express my deep sense of gratitude and thankfulness to my esteemed teacher, mentor and Guide **Prof. Dr. S. SHOBHA,** M.D., D.G.O., for her invaluable guidance and constant help at every stage of this work. She has been a great inspiration for me for the fulfilment of this work.

My deep gratitude goes to my beloved **Prof. Dr. G. GEETHA,** M.D., D.G.O., **Prof. Dr. T. K. SHAANTHY GUNASINGH,** M.D., D.G.O., **Prof. Dr. V.SUMATHY,** M.D., D.G.O., **Prof. Dr. P. S. JIKKI KALAISELVI** M.D., D.G.O., Department of obstetrics and gynaecology in conducting this study.

I thank My Co-Guide **Dr. V. VANITHA,** M.D (O & G) for guiding me to proceed with this study.

I am grateful to our beloved **Dean, Prof. Dr. P. RAMAKRISHNAN,** M.D., D.L.O., for permitting me to utilize the hospital resources for this work.

I wish to render my deep appreciation to **Mr. Padmanaban,** Statistician, who has taken great pains in helping me with statistical analysis of data.

I thank all my Assistant Professors, My Colleagues, Laboratory Technicians and Patients, without whom this study would have not been possible.

Finally I express my sincere thanks to all My Family Members.

DECLARATION

I, **Dr. E. GEETHANJALI** solemnly declare that this dissertation **"A STUDY TO DETERMINE THE INCIDENCE OF OBSTETRIC CHOLESTASIS AND TO EVALUATE PREGNANCY OUTCOME IN WOMEN WITH OBSTETRIC CHOLESTASIS"** was prepared by me at Government Kilpauk Medical College and Hospital, Chennai, under the guidance and supervision of **Prof. Dr. S. SHOBHA,** M.D., D.G.O., Professor of Obstetrics and Gynaecology, Govt. Kilpauk Medical College and Hospital, Chennai.

This dissertation is submitted to **The Tamil Nadu Dr. M.G.R. Medical University, Chennai** in partial fulfillment of the University regulations for the award of the degree of **M.D. Branch II (Obstetrics and Gynaecology).**

Place : Chennai
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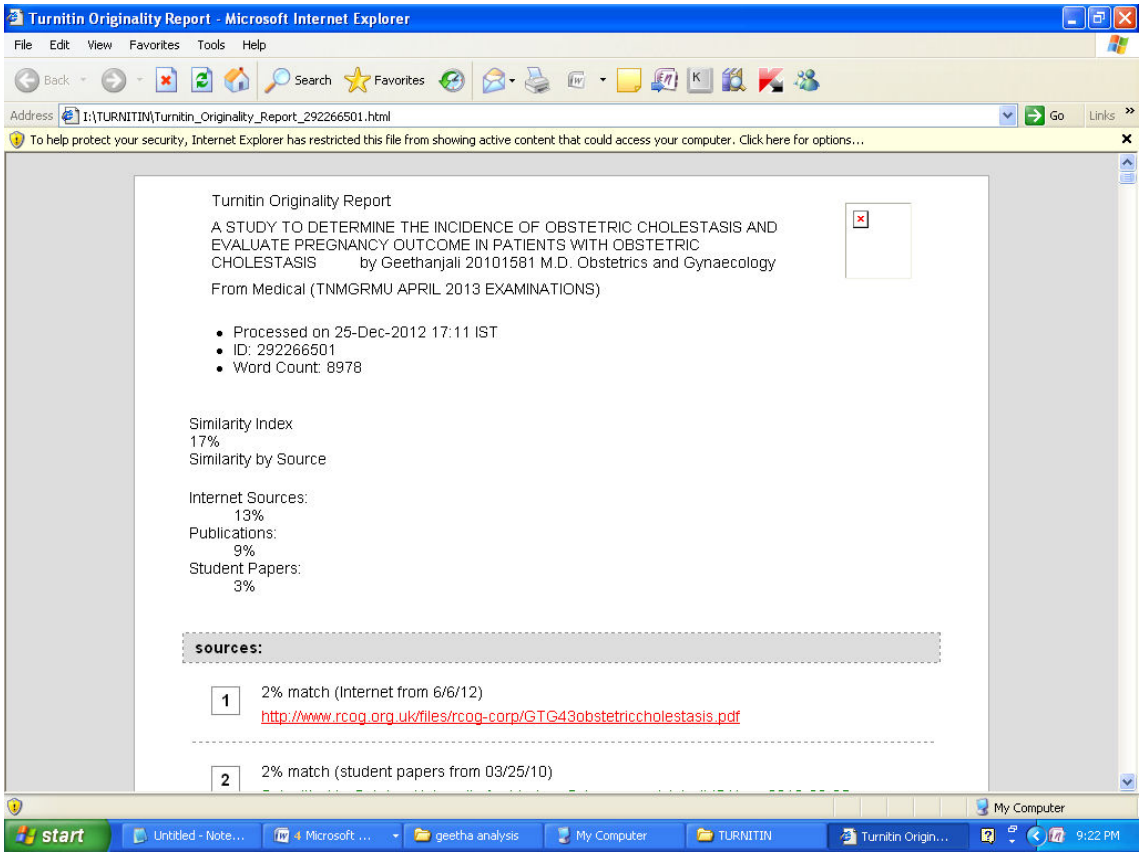

ABBREVIATIONS

1. AFI – Amniotic fluid index.
2. AFLP – Acute fatty liver of pregnancy.
3. ALP – Alkaline phosphatase.
4. ALT – Alanine aminotransferase.
5. AST – Aspartate aminotransferase.
6. CTG – Cardiotocogram.
7. ELISA – Enzyme linked immunosorbent assay.
8. FFP – Fresh frozen plasma.
9. GGT – Gamma glutamyltranspeptidase.
10. IHCP – Intrahepatic cholestasis of pregnancy.
11. IUD – Intrauterine death.
12. LDH – Lactate dehydrogenase.
13. LN – Labour naturale.
14. LSCS – Lower segment caesarean section.
15. NICU – Neonatal intensive care unit.
16. TGL – Triglyceride.
17. UDCA – Ursodeoxycholic acid.

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INTRODUCTION

Obstetric cholestasis is a liver disease unique to pregnancy. Once assumed to be a benign condition, its significance has been highlighted only recently due to associated maternal & perinatal morbidity & mortality.

Its incidence varies with the population. The incidence of obstetric cholestasis has been difficult to estimate as a result of likely under reporting or failure to recognise mild cases. So, careful history taking and simple biochemical tests will be helpful in early diagnosis and appropriate intervention in these patients. This will lead to significant reduction in maternal and perinatal morbidity and mortality.

As obstetric cholestasis rarely presents with jaundice, and with non specific symptoms such as pruritus and disturbed sleep, it is difficult to diagnose.

AIM OF THE STUDY

To determine the incidence of obstetric cholestasis, study the course of pregnancy and evaluate pregnancy outcome in women with obstetric cholestasis.

Pregnancy outcome is evaluated in terms of term/preterm/post term delivery, Mode of delivery, Meconium staining of liquor, Birth weight of baby, NICU admissions, Fetal growth restriction.

The efficacy of UDCA in controlling pruritus is also evaluated.

REVIEW OF LITERATURE

EPIDEMIOLOGY

Due to significant genetic influence, the incidence varies with population.Cholestasis is uncommon in North America,with an incidence of approximately 1 in 500 to 1000 pregnancies.

In Israel, the incidence reported by Sheiner and associates (2006) is approximately 1 in 400.

In Italy,the incidence is 1%.In Sweden, it is 1.5% and in Chile,it is 4%.In England,it affects 0.7% of pregnancies in multi-ethnic populations and 1.2% to 1.5% of pregnancies of Indian-Asian or Pakisthani-Asian origin.[1]

There are only limited studies in India and particularly in South India and even the few studies which have been conducted have small sample size and hence the reliability is very low.

PATHOGENESIS

Cholestasis (failure of bile formation) represents an exaggerated response of the liver to the normal increase in endogenous estrogens during pregnancy.Leslie and colleagues (2000) reported that plasma estrogen levels are *decreased* in affected women[2].Bile acids are incompletely cleared by the liver and accumulate in plasma.

There is a role for mutations in the genes that control hepatocellular transport systems [3].One of such genes is *Multidrug resistance 3 (MDR 3)* gene found with progressive familial intrahepatic cholestasis. [4].This genetic predisposition shows autosomal dominance.

The elevation in maternal levels of bile acids impairsthe normal feto-maternal transfer and excess bile acids with abnormal profiles accumulates which are toxic to the fetus.

The drugs which decrease the canalicular membrane transport of bile acids aggravate this disorder.There are few case reports of cholestatic jaundice in pregnant women taking azathioprine after renal transplantation.

The end effect is that, bile acids are incompletely cleared and they accumulate in plasma. Even before bile acid levels increase, associated dyslipidemia is evident.[5]

Hyperbilirubinemia is due to accumulation of conjugated pigment, but the total level never exceeds 4 to 5 mg%. Liver biopsy shows mild

cholestasis with bile plugs in hepatocytes and canaliculi of centrilobularregions, but *without inflammation or necrosis* .The changes disappear after delivery. Similar changes are seen in women using Oral contraceptive pills and cyclically during menstruation.[1]

SYNTHESIS OF BILE ACIDS [6]

Bile consists of a watery mixture of organic and inorganic compounds. Phosphatidyl choline and bile salts are quantitatively the most important organic components of bile. Bile can either pass directly from the liver where it is synthesized into the duodenum through the common bile duct, or be stored in the gall bladder when not immediately needed for digestion.

Structure of bile acids:-

The bile acids contain 24 carbons, with two or three hydroxyl groups and a side chain that terminates in a carboxyl group. The carboxyl group has a pKa of about six and hence it is not fully ionised at physiologic pH and so, it is termed as" bile acid". The bile acids are amphipathic in that the hydroxyl groups are in α orientation and the methyl groups are in βorientation. Therefore the molecules have a polar and a nonpolar face,and can act as emulsifying agents in the intestine, helping prepare dietary triacylglycerol and other complex lipids for degradation by pancreatic digestive enzymes.

Synthesis of bile acids:-

Bile acids are synthesized in the liver by a multistep, multiorganelle pathway in which hydroxyl groups are inserted at specific positions on the

steroid structure, the double bond of the cholesterol B ring is reduced, and the hydrocarbon chain is shortened by three carbons, introducingcarboxyl groups at the end of the chain. The most common resulting compounds, thecholic acid and chenodeoxycholic acid are called *primary bile acids.*

Synthesis of bile salts:-

Before the bile acids leave the liver, they are conjugated to a molecule of either glycine or taurine (an endproduct of cysteine metabolism).These new structures are called bile salts and include glycocholicacid, glycol chenodeoxycholicacid, taurocholic, tauro chenodeoxycholicacid. The ratio of glycine and taurine forms in the bile is 3:1.Bile salts are more effective detergents than bile acids because of their enhanced amphipathic nature. Therefore, only the conjugated forms – that is, the bile salts – are found in the bile. Individuals with genetic deficiencies in the conversion of cholesterol to bile acids are treated with exogenously supplied chenodeoxycholic acid.

Bile salts provide the only significant mechanism for cholesterol excretion,both as a metabolic product of cholesterol and as a solubiliser of cholesterol in bile.

Action of intestinal flora on bile salts:-

Bacteria in the intestine can remove glycine and taurine from bile salts,regenerating bile acids. They can also convert some of the primary bile acids into secondary bile acids by removing a hydroxyl group producing deoxycholic acid from cholic acid and lithocholic acid from chenodeoxycholic acid.

Enterohepatic circulation:-

Bile salts are secreted into the intestine are efficiently reabsorbed (greater than 95%) and reused. The mixture of primary and secondary bile acids and bile salts is absorbed primarily in the ileum. They are actively transported from the intestinal mucosal cells into the portal blood, and are efficiently removed by the liver parenchymal cells. The liver converts both primary and secondary bile acids into bile salts by conjugation with glycine or taurine, and secretes them into bile. The continuous process of secretion of bile salts into bile, their passage through duodenum where some are converted into bile acids and their subsequent return to the liver as a mixture of bile acids and salts is termed as enterohepatic circulation.

Between 15 and 30 g of bile salts are secreted from the liver into the duodenum each day, yet only about 0.5 g is lost daily in the feces. Approximately 0.5 g/day is synthesized from cholesterol in the liver to replace the lost bile acids.[10]

CLINICAL PRESENTATION [7]

Generalised pruritus, which is insidious in onset is the predominant symptom. There are no accompanying skin changes unless there are excoriations from scratching. Mostly seen in second half of pregnancy. The pruritus in this condition, predominantly involves palms and soles but may also involve arms, legs, chest, back and face. It may be severe to such an extent, it disturbs sleep.

Occasionally, it manifests even earlier. Kirkinen and Rynnanen (1995) described a women at 13 weeks with cholestasis associated with hyperplacentosis and triploid fetus.

Pruritus usually precedes laboratory findings by a mean of 3 weeks and sometimes by months [2].

Other features of cholestasis like dark urine, pale stools may also be present. Mild icterus may be present but it is rare. It is present in about 10% of cases. The other liver symptoms like nausea, vomiting and abdominal pain are typically absent [7].

LIVER FUNCTION TESTS IN PREGNANCY [7]

LFT	NON PREGNANT	1ST TRIMESTER	2ND TRIMESTER	3RD TRIMESTER
Bilirubin (μmol/L)	0 - 17	4 - 16	3 – 13	3 - 14
AST(IU/L)	7 - 40	10 - 28	11 – 29	11 - 30
ALT(IU/L)	0 - 40	6 - 32	6 – 32	6 - 32
GGT(IU/L)	7 - 41	5 - 37	4 – 43	3 - 41
ALP(IU/L)	20 - 125	6 - 375	Increases progressively To term	
Albumin(g/L)	35 - 55	Falls by 10g/L	Increases progressively To term	
Total proteins (g/L)	65 - 80	Falls by 10g/L	Increases progressively To term	
Globulin(g/L)	30 - 50	Increases progressively To term		
Fibrinogen(g/L)	2 - 4	Increases progressively To term		
Cholesterol (mol/L)	4 – 6.5	Increases progressively To term		
TGL(nmol/L)	<1.5	Increases progressively To term		

LIVER FUNCTION TESTS IN OBSTETRIC CHOLESTASIS [8]

- Bilirubin – Total bilirubin never exceeds 4-5mg/dl.
- Serum ALP is usually elevated.
- Serum transaminases are moderately elevated and never exceed 250 IU/L.
- Serum levels of cholicacid,chenodeoxycholic acid and total 3α hydroxyl bile acids are elevated from 10 to 100 fold in patients with IHCP.
- As the cholestasis of pregnancy progresses till delivery, the biochemical parameters i.e., liver function tests also worsen as pregnancy advances.
- Biochemical abnormalities usually return to pre pregnant levels within 2 weeks after delivery. If the abnormality persists after 2 weeks of delivery, other diagnosis should be considered.
- Occasionally, serum cholesterol levels may be elevated in intrahepatic cholestasis

URSO DEOXY CHOLIC ACID [9]

- Category B drug.
- It is a naturally occurring bile acid used orally to dissolve gall stones.
- It is a hydroxyl epimer of chenodeoxycholic acid.
- Absorbed from small intestine and extracted and conjugated by liver.
- Although 30% - 50% of a dose may enter the systemic circulation, continuous hepatic uptake keeps ursodiol blood levels low and uptake by tissues other than liver is nil.
- These factors combined with tight binding to albumin possibly indicate that placental passage to fetus does not occur.
- Mechanism of action :
- Acts primarily by inhibiting intestinal cholesterol absorption. It has inconsistent effect on HMG-CoA reductase.
- It also inhibits hepatic cholesterol synthesis but to a lesser extent. It promptly reduces cholesterol secretion in bile.
- It itself lowers the cholesterol saturation index of bile.
- It promotes solubilisation by liquid crystal formation.
- For its action, gall bladder should be functional – if the bile is not entering gall bladder, it will not be able to solubilise gall stones.
- Ursodiol is effective in the treatment of IHCP and its use for this purpose appears to be low risk for the fetus.

- Dose – 8 to 10 mg/kg/day.
- Other uses – It is primarily being used as a gallstone stabilising agent.It has been used successfully in the treatment of intrahepatic cholestasis of pregnancy, biliary fistula and liver disease. They are a constituent of many combination formulations.
- Although chenodeoxycholic acid and ursodeoxycholic acid are used for similar purposes, their mechanism of action is different.

OTHER DRUGS IN TREATMENT OF OBSTETRIC CHOLESTASIS[10]

There is no evidence that any specific treatment improves fetal or neonatal outcomes. All such therapies should be discussed with the individual woman with this in mind.

Topical emollients

Topical emollients are safe but their efficacy is unknown. Bland topical options include calamine lotion and aqueous cream with menthol. There are no trial data to support or refute the use of these products. They are safe in pregnancy and clinical experiencesuggests that for some women they may provide slight temporary relief of pruritus.

Systemic treatment

Systemic treatments aimed at relieving pruritus include cholestyramine, a poorly tolerated bile acid-chelating agent, which may improve pruritus in some women but may also exacerbate vitamin K deficiency(which has been associated with fetal intracranial haemorrhage). Cholestyramine has not been subjected to randomised trials and is not in clinical use. Antihistamines such as chlorphenamine may provide some sedation at night but do not have a significant impact on pruritus. Activated charcoal and guargum do not relieve pruritus.

S-adenosyl methionine:

There is insufficient evidence to demonstrate whether S-adenosylmethionine (SAMe) is effective for either control of maternal symptoms or for improving fetal outcome, and it is not recommended.

Plasmapheresis:

Warren and associates (2005) reported dramatic relief in a women with refractory pruritus who was treated by plasmapheresis and 5% albumin replacement.

OBSTETRIC CHOLESTASIS AND PREGNANCY OUTCOMES [11]

Pregnancy outcomes are adverse in women with cholestaticjaundice. There are increased rates of meconium staining of liquor. There is an increased incidence of gall stones.

The incidence of preterm labour is 60%.Fetal distress and meconium staining of liquor occurs in severe cholestasis. Surprisingly, IUDs and still births are seen in clinically mild cholestasis. The risk for IUD and fetal distress increase near term.

The mechanism(s) of preterm labour, fetal death and meconium staining are not known but these events are attributed to elevated bile acids in circulation which increase uterine contractions and fetal colonic muscle contractions.

CTG is normal for up to 2 days before fetal demise. Gorelik and colleagues (2006) [12] suggest that bile acids may cause fetal cardiac arrest after entering cardiomyocytes in abnormal amounts. Using fetal myocyte cultures, they showed expression of several genes that may play a role in bile transport.

PRURITUS IN PREGNANCY [8]

The causes of pruritus in pregnancy are,

1. Pruritic urticarial papules and plagues of pregnancy.
2. Prurigo of pregnancy.
3. Herpes gestationis / pemphigoid gestationis.
4. Intrahepatic cholestasis of pregnancy.
5. Pruritic folliculitis of pregnancy.
6. Non primary pruritic conditions like atopic dermatitis and contact dermatitis.

The characteristic feature of pruritus in intrahepatic cholestasis of pregnancy is that it predominantly involves palms and soles, is not associated with skin rashes except for those excoriations which occur due to scratching. It has tremendous adverse psychological impact on the mother as it disturbs her sleep. This pruritus responds well to UDCA. Topical emollients may have some use. This pruritus completely resolves within 24 - 48 hours after delivery.

DIFFERENTIAL DIAGNOSIS[11]

The differential diagnosis of intrahepatic cholestasis of pregnancy involves other cholestatic conditions such as,

1. Primary biliary cirrhosis.
2. Primary sclerosing cholangitis.
3. Benign recurrent intrahepatic cholestasis (BRIC).
4. Viral hepatitis.
5. Biliary obstruction.

Primary biliary cirrhosis and primary sclerosing cholangitis are autoimmune disorders and they have anti nuclear and anti smooth muscle antibodies. Jaundice is very severe in these patients and dark yellow conjunctiva is the most striking feature.

Benign recurrent intrahepatic cholestasis closely resembles intrahepatic cholestasis and it is very difficult to differentiate between these two conditions.

Viral hepatitis is easily diagnosed by viral marker assays.

Ultrasonogram diagnoses biliary obstructions with utmost ease.

FETAL MONITORING [12]

Antepartum fetal monitoring is an important aspect in antenatal care in patients with obstetric cholestasis as the fetus bears the brunt of this disease.

An admission CTG should be done as a baseline. It is not necessary to admit all the patients with obstetric cholestasis, but biweekly CTG with AFI should be done. If there is any abnormality, pregnancy should be terminated irrespective of gestational age.

In case of foetuses which fare normal, some advise to carry pregnancy to term and some advise elective termination at 38 weeks. Neonatal morbidity and mortality are mainly due to meconium staining of liquor, pretermdeliveries, low birth weight and preterm premature rupture of membranes.

During labour, continuous intrapartum electronic fetal monitoring should be available. As post partum haemorrhage is found to be slightly high in patients with obstetric cholestasis, these patients should be carefully watched for postpartum haemorrhage.

LIVER IN PREGNANCY [13]

Liver size remains normal in pregnancy. Hepatic blood flow and hence the diameter of portal vein increases during pregnancy. Histological evaluation of liver biopsies, including examination under electron microscope, has shown no distinct morphological changes in normal pregnant women.

Leucine aminopeptidase is a proteolytic liver enzyme whose serum levels are increased with liver disease. Its activity is markedly elevated in pregnant women. The increase however results from the appearance of a pregnancy specific enzyme(s) with distinct substrate specificities. Pregnancy induced aminopeptidase has oxytocinase and vasopressinase activity which occasionally causes transient diabetes insipidus.

LIVER DISEASES IN PREGNANCY [11]

Liver diseases encountered in pregnancy may be coincidental, related to pregnancy or may be present even before pregnancy.

Liver disorders related to pregnancy:

These diseases are induced due to this specific condition, i.e., pregnancy and they resolve after delivery.

These are,

1. Intrahepatic cholestasis of pregnancy.
2. Acute fatty liver of pregnancy.
3. Hyperemesis gravidarum (Hepatic dysfunction).
4. Severe pre-eclampsia (Hepatocellular damage).

Intrahepatic cholestasis of pregnancy:

- ❖ In most of the cases, it is seen in the second half of pregnancy.
- ❖ Important histological finding – Intrahepatic cholestasis with centrilobular bile staining without inflammatory cells or proliferation of mesenchymal cells.
- ❖ This is because of high estrogen levels in susceptible women.
- ❖ Incomplete clearing of bile acids in the liver which accumulate in plasma.[19]

Clinical features :

- ❖ Presenting symptom in most of the cases is pruritus, which is generalised.
- ❖ The pruritus in this condition is not accompanied by skin changes except that due to skin excoriation due to scratching.
- ❖ Icterus is rare.
- ❖ Liver enzyme levels are elevated, especially those of serum alkaline phosphatase and transaminase.

Management :

Pruritus is extremely troublesome which most often disturbs sleep. This can be managed with orally administered anti histaminics and Cholestyramine.

Acute fatty liver of pregnancy :

- ❖ Incidence – 1 in 10,000 to 1 in 15,000 pregnancies.
- ❖ An uncommon complication that has proved fatal to both the mother and the fetus.
- ❖ Maternal mortality rate – 18%.
- ❖ Fetal mortality rate – 23%.
- ❖ An interesting fact about AFLP is that it is more common in nulliparous ladies and in those carrying twins or male fetus.[18]

Etiopathogenesis :

Mitochondrial abnormalities of fatty acid oxidation which are recessively inherited predispose a women to this condition. The enzyme, long chain 3-hydroxy acyl CoA dehydrogenase (LCHAD) is suggested.

This enzyme is one of the four enzymes which breaks down long chain fatty acids in the liver. Deficiency of this enzyme results in increased accumulation of long chain fatty acids in the liver.

The most common mutations have been localised to a G1528C mutation in over 60% of cases and an E474Q mutation in 19% of the cases.These mutations are located on the mitochondrial trifunctional complex on chromosome 2.

An individual heterozygous for this mutation, will have no abnormalities of fatty acid oxidation under normal circumstances. But, when a heterozygous women has a fetus which is homozygous for this mutation, it will be unable to oxidise long chain fatty acids. These long chain fatty acids accumulate in the fetus and are transferred to the mother via the placenta. As a result, triglycerides accumulate within maternal hepatocytes (especially in mitochondria) resulting in impaired liver function and in its grave form, to liver failure. Delivery of the fetus terminates this process and hence maternal liver function improves after delivery.

Clinical features:

It manifests usually in the third trimester, late in pregnancy. The peak period of manifestation is 36 – 37 weeks. Sometimes it may occur even after delivery. Malaise, anorexia, vomiting, epigastric pain are seen. Coagulation failure is an associated feature.

Jaundice is common but not invariable. Nearly 50% of these patients will have signs of pre eclampsia. Maternal mortality rate is very high.autopsy shows a *small soft, yellow and greasy liver.*

The size of the liver is usually normal or sometimes small. Pruritus is uncommon and would suggest a different liver problem like intrahepatic cholestasis of pregnancy.

Liver function tests:

Moderate elevations of ALT and AST, around 300U/L, are usual but some patients may have very high (1000 U/L) and some patients may have normal values. Alkaline phosphatase and serum bilirubin are elevated.

Histology

Swollen hepatocytes, cytoplasm is filled with microvesicular fat with central nuclei. All these changes have a *centrilobular distribution.*

Differential diagnosis [12]

1. HELLP syndrome.
2. Viral hepatitis.
3. Drug induced hepatitis.

Presence of hypoglycaemia, prolongation of prothrombin time andabsence of thrombocytopenia differentiates this condition from HELLP syndrome.

Treatment :

Delivery of the fetusis the cure for this condition. Appropriate supportive measures should be kept ready while making arrangements for urgent delivery.

Screening :

As early diagnosis improves outcome, screening for LCHAD deficiency should be done in all babies born to mothers who are diagnosed to be having AFLP.

Obtaining chorionic villous sampling and amniocentesis can assist in prenatal diagnosis if foetuses with LCHAD deficiency.

Genetic counselling:

AFLP can recur in subsequent pregnancies and hence genetic counselling should be offered.

Hyperemesis gravidarum :

Incidence – 0.2 – 1.6 per 1000 deliveries. In this condition, nausea and vomiting occur in sufficient levels to cause dehydration. It usually occurs during first trimester of pregnancy but may occur as late as 20^{th} week.

Due to excessive vomiting, hepatic dysfunction occurs which usually requires hospitalisation. Abnormal liver enzyme levels have been reported in up to 50% of patients hospitalised for hyperemesis.

Etiopathogenesis :

Genetic predisposition and high circulating levels of estrogen are thought to be causative factors.

Liver function tests :

There may be mild hyperbilirubinemia and liver transaminase levels are elevated in half of the patients. Bilirubin levels are usually less than 4 mg/dl with elevations in both direct and indirect fractions. Alkaline phosphatase levels are increased to about twice the normal value and aminotransferase levels may be as high as 200 U/L.[19]

The mechanism of hyperbilirubinemia is unknown. This condition is most probably related to malnutrition and impaired excretion of bilirubin, because laboratory test results show that the values return to normal within days after resumption of adequate nutrition and restoration of fluid balance.

Treatment:

Correct diagnosis of the cause and its correction usually improves this condition. Psychological support is often not given much importance which is of paramount importance in the present changing lifestyle of people.

Fetal outcome :

The mean birth weight of babies in patients with severe hyperemesis gravidarum, defined as loss of more than 5% of birth weight is significantly lower than that of the offspring of women with mild hyperemesis gravidarum.

Pre eclampsia and eclampsia :

Hepatic dysfunction is seen in severe pre eclampsia or eclampsia. The pathological lesion is periportal haemorrhage, fibrin deposition and hepatocyte necrosis. The degree of dysfunction and histological changes vary considerably.[19]

The characteristic epigastric or substernal pain called pre eclamptic angina is attributed to hepatic subcapsular stretching.

Subcapsular hematoma and hepatic rupture rarely develop. The hepatic complications that develop due to pre eclampsia and eclampsia are grouped together as **HELLP** syndrome. *Weinstein in the year 1982 coined the term HELLP*. HELLP syndrome is usually associated in 5 – 10% of patients with pre eclampsia. Sometimes, it may arise in the absence of either hypertension or proteinuria. The exact cause for HELLP syndrome remains unclear, but vascular endothelial damage plays an important role.

H – Hemolysis.

EL – Elevated liver enzymes.

LP – Low platelet count.

Criteria for diagnosis

Hemolysis :

1. Abnormal peripheral smear.
2. Bilirubin >/= 1.2 mg/dl.
3. LDH >/= 600 IU/L.

Elevated liver enzymes :

1. SGOT >/= 72 IU/L.

2. LDH >/= 600 IU/L.

Low platelets :

Platelet count </= 100,000 cells/cubic mm.

Classification based on platelet count :

1. Class 1 - < 50,000/cubic mm.
2. Class 2 – 50,000 – 100,000/cubic mm.
3. Class 3 – 100,000 – 1,50,000/cubic mm.

Treatment of HELLP syndrome :

- ❖ Stabilise the general condition.
- ❖ Fresh blood,FFP.
- ❖ MgSo4 for seizure prophylaxis.
- ❖ Anti hypertensive for BP control.
- ❖ High dose corticosteroid treatment :
- ❖ Dexamethasone 10 mg i.v , 2 doses 6 hours apart, totally 4 doses.
- ❖ Dexamethasone 6 mg i.v 2 doses 6 hours apart, totally 4 doses.

Platelet transfusion is indicated if the platelet count is less than 20,000/cubic mm. Treatment of liver rupture is that of laparotomy, drainage of hemoperitoneum and subhepatic packing.[19]

The placenta is solely responsible for the hypertensive changes and hence the curative treatment for this hepatic dysfunction due to pre eclampsia is the delivery of the placenta.

Laboratory abnormalities peak 24 to 48 hours post partum and hepatic enzyme abnormalities and platelet counts come to normal levels in 2 to 3 days.

Differentiation of AFLP from HELLP syndrome may be very difficult, but the treatment, i.e., prompt delivery and supportive care is same in both the cases.

Liver diseases complicating pregnancy

Viral hepatitis is the liver disease most often encountered in pregnant women. There are five distinct types of viral hepatitis. They are hepatitis A,B,C,D,E ; Hepatitis D is caused by the B – associated delta agent.

Clinical Features :

In clinically apparent cases of viral hepatitis, non specific symptoms like nausea, vomiting, headache and malaise precede jaundice by 1 to 2 weeks. Low grade fever is more common with hepatitis A. When jaundice develops, symptoms improve. There may be pain and tenderness over the liver.[18]

Laboratory features :

Serum aminotransferase levels – their levels vary and do not correspond with disease severity. Peak levels of 400 – 4000 U/L are usually reached by the time when jaundice develops. *Serum bilirubin* – the peak

levels of serum bilirubin are usually at 5 to 20 mg/dl and they continue to rise despite fall in enzyme levels.

Management :

There is no difference in the management protocol between pregnant and non pregnant patients. But, pregnant women with hepatitis require hospitalisation and delivery at a well equipped hospital because the maternal and perinatal morbidity and mortality is high.

Termination of pregnancy in hepatitis is practised only for obstetric indications. Hepatitis by itself is not an indication for termination of pregnancy.

Maternal complications :

Incidence is more common in the second and third trimesters of pregnancy. Hepatic failure is more common in pregnancy. In patients with poor socio economic status, malnutrition is more prevalent and this in turn predisposes to increased morbidity due to liver failure.[18]

Hepatic coma is a fatal complication and it is usually encountered in patients who die before delivery. In patients after delivery, post partum haemorrhage is a fatal complication.

Pregnancy in women with pre existing liver disease [13]

The pre existing liver diseases may be

1. Autoimmune chronic active hepatitis.
2. Chronic viral hepatitis.
3. Primary biliary cirrhosis.
4. Cirrhosis.
5. Cholestatic disorders.
6. Wilsons disease.
7. Hepatic adenoma/focal nodular hyperplasia.

Effect of pregnancy on pre existing liver disease:

Pregnancy is unusual in patients with chronic liver disease as there is a high prevalence of infertility among these group of patients. Fertility becomes near normal when cirrhosis is well compensated and when there is good improvement in autoimmune diseases due to treatment with steroids.

The degree of hepatic impairment determines the risk for the mother during pregnancy. Haemorrhage from esophageal varices is the most significant complication of cirrhosis in pregnancy.The increased blood volume and flow through the azygos system that are a part of any normal pregnancy raise the pressure in the esophageal veins. In established cirrhosis, this increases variceal size and the likelihood of bleeding.

Pre-existing chronic liver disease requires careful monitoring of the patient, as the disease may worsen during pregnancy.Careful monitoring of the fetus is of paramount importance.Most often,women with pre-existing liver disease are able to carry the fetus safely to term.[18]

Autoimmune chronic active hepatitis (CALD):

Flare ups has been reported during pregnancy.However,it is not clear whether the flare ups of CALD have actually been induced by pregnancy,since autoimmune hepatitis is a disorder characterised by exacerbations and remissions.

Prednisone and azathioprine are usually used to treat CALD.These can be used safely during pregnancy, and they have no adverse effects on the fetus. Pregnant women who have CALD (with or without therapy) have a higher incidence of both stillbirths and premature delivery.

Chronic viral hepatitis :

There is little evidence that pregnancy influences the clinical course of either chronic active or chronic persistent viral hepatitis. Sometimes, worsening of chronic hepatitis B and hepatitis C has been reported.

Primary biliary cirrhosis (PBC):

Pregnancy often leads to an increase in the biochemical parameters of cholestasis in women with primary biliary cirrhosis. Clinically, PBC does not exhibit an accelerated course during pregnancy.

After delivery, these abnormalities return to their normal values. As PBC tends to occur in older women, PBC and pregnancy are not often seen as concomitant problems in same patient.

Cirrhosis :

Women with cirrhotic liver may carry a pregnancy to term without any problem. But the fertility rate is very low in women with cirrhosis. However, some cases of worsening hepatic function, jaundice and hepatic failure have been reported in pregnant women with cirrhosis.

The risk of variceal haemorrhage is increased in pregnant women with cirrhosis. The mode of treatment for variceal haemorrhage during pregnancy

is endoscopic ligation or sclerotherapy. Women with cirrhosis have higher rates of still births and premature deliveries.

Cholestatic disorders :

Patients with Dubin-Johnson syndrome demonstrate an increase in conjugated bilirubin during pregnancy. Patients with Gilbert syndrome do not develop an increase in unconjugated bilirubin during pregnancy.

Patients with the rare syndrome of benign recurrent intrahepatic cholestasis (BRIC) usually develop jaundice during pregnancy. Unaffected first degree relatives of patients with BRIC develop cholestasis during pregnancy.

Wilson's disease : [14]

It is a very rare disease and it is less commonly encountered during pregnancy. It is due to a genetically transmitted disturbance in copper metabolism that leads to copper toxicity and death, usually before the age of 30.

Treatment – Penicillamine, which is a copper chelator, in a dose of 0.75 – 1 gm/day. This dosage is safe and is not associated with any untoward side effects in the fetus. Compliance to this drug is very much important as its discontinuation during pregnancy has been associated with worsening of hepatic disease.

Hepatic adenoma or focal nodular hyperplasia :

These are very common hepatic tumors during pregnancy. Although these tumors may enlarge and rupture during pregnancy,it is a very rare event.

HISTORICAL REVIEW

J.Goreth et al and C Williamson et al, from National Heart and Lung Institute and Institute of Reproductive and Development biology at the Imperial college, London conducted a study to associate obstetric cholestasis and still birth and found significant correlation, $p < 0.05$ between these two. The sample size in this study was 72 and this study was conducted over a period of two years.[15]

Pilot study for a trial of UDCA and/or early delivery for obstetric cholestasis. This study was conducted in Nottingham, England. It was multi centered, double blinded, randomised, controlled, factorial design trial. The investigating medical officer, pharmacist, and the trial participant will be blind to know to which group they are allocated. The study was conducted in 6 United Kingdom Centres and women with intrahepatic cholestasis of pregnancy will be followed up for 18 months.[16]

Comparison group A – UDCA Vsplacebo. Comparison group B – Planned delivery at 37 weeks of gestation Vs awaiting spontaneous delivery till term. Sample size – 125.This trial concluded that UDCA and early term delivery decreased still birth rate and fetal complications like meconium staining of liquor, respiratory distress and low birth weight.

Roncaglia N et al and Arreghini A et al from the department of Obstetrics and Gynaecology, Monza, Italy studied the outcome of patients with obstetrics with active management. This study was conducted between January 1989 and December 1997.All women with obstetric cholestasis underwent transcervical amnioscopy after 36 weeks of gestation for assessment of colour of amniotic fluid and they were also subjected to antepartum fetal monitoring, i.e., biweekly non stress test and amniotic fluid index.[17]

In severe cases, amniocentesis was done before 36 weeks for assessment of fetal lung maturity and amniotic fluid colour assessment. Induction of labour was done earlier before 37 weeks in the presence of adverse fetal parameters. The outcome of pregnancy was compared between the population with obstetric cholestasis and the general population.

Results: The incidence of obstetric cholestasis was 1%.Mean gestational age at diagnosis was at 34 weeks. Meconium staining of liquor in 16%.The meconium staining of liquor before 37 weeks was significantly higher in patients with obstetric cholestasis than in the general population (17.9% Vs 2.9%).The rate of caesarean section was equal in both groups (15.1% Vs 16%).

Conclusion : In pregnant patients with obstetric cholestasis, practising a protocol, which includes a search for meconium staining of liquor and elective termination of pregnancy at 37 weeks of gestation and antepartum fetal monitoring, significantly reduces the still birth rate without an increase in caesarean section rate.

He j et al,Chen et al,Liang C et al from the department of Obstetrics, Women' shospital, Hangzhou, China conducted a retrospective analysis of 21 cases of intrahepatic cholestasis of pregnancy whose foetuses succumbed to intrauterine death. This study was conducted from January 1999 to December 2010.[18]

Results :

- The mean age of patients with IHCP with fetal death was 30.2+/-4.6 years.
- Out of 21 cases, 20 patients were having singleton pregnancy 1 was twin gestation.
- All cases of intrauterine death occurred in third trimester.
- The average gestational age at which fetal death occurred was 33.8 weeks of gestation.
- Perinatal mortality rate in patients with IHCP was 0.418%.
- All 21 patients had normal vaginal delivery.

- ❖ Serum glycocholic acid levels were increased in all the 21 cases.
- ❖ 18 cases had grade 3 meconium staining of liquor in amniotic fluid.
- ❖ Conclusion :
- ❖ Intrauterine fetal death in patients with IHCP occurs after the onset of uterine contractions,either spontaneous or induced.
- ❖ Uptodate, there is no valid investigation by which we can pick up impending fetal distress.
- ❖ Before elective termination of pregnancy, an accurate assessment of the gravity of the disease and fetal maturity should be done.

Roncaglia et al, Locatelli et al, Arreluni et al conducted a randomised control trial comparing the efficacy of S-Adenosyl methionine and UDCA in improving biochemical parameters in IHCP. Sample size – 46.Period of study was from june 1996 to December 2001.The study concluded that in the relief of pruritus, in patients with IHCP, UDCA and S-Adenosyl methionine were equally effective. Concerned to the improvement in biochemical parameters, UDCA is more effective than S-adenosyl methionine.[19]

Brites D et al conducted a study from university of Lisbon, Portugal in the year 2002 on the changes in the bile acid balance in the mother and the fetus and its improvement by the use of UDCA. This study concluded

that UDCA is effective in reducing maternal and fetal bile acids and hence in improving neonatal outcome.[20]

Wong LF et al,Shallow H et al, O' Connel MP et al, conducted a comparative study on the outcome of IHCP over a 27 months period, from the Department of Obstetrics and Gynaecology, Dublin, Ireland.[21]

Sample size – 753.The patients were divided into two groups. Obstetric cholestasis and idiopathic pruritus of pregnancy groups.The idiopathic pruritus of pregnancy group served as controls.

The percentage of preterm labour was 18% Vs 7.7% of controls. Out of 151 mothers with obstetric cholestasis,48.3% had total bile acids between 11-33.9 μmol/L,21.2% had total bile acids > 40 μmol/L and the rest of 30.5% had total bile acids in the range of 6 and 10.9 μmol/L. In patients with obstetric cholestasis and who had preterm delivery, all had increased total bile acids more than 11 μmol/L.

This study concluded that IHCP increases preterm delivery, induction of labour, NICU admissions, and low birth weight babies. A cut off value for serum bile acids for diagnosis of IHCP is more than 11 μmol/L.

Castano G et al, Lucangioli S et al did a study on serum bile acid profiles by the method of capillary electrophoresis in obstetric cholestasis.

They did the study from Gastroenterology section, J.M. Pennahospital, Argentina.[22]

Asymptomatic hypercholanaemia of pregnancy is the elevation of serum bile acids above the cut off value in healthy normal women in pregnancy.This shows that serum bile acids are elevated in a substantial proportion of normal pregnancies. So, it becomes important to distinguish AHP from IHCP by studying serum bile acid profiles in these patients.

The study concluded that the women with obstetric cholestasis had elevated serum bile acids, free/ conjugated, lithocholic acid (LCA), cholic acid (CA), chenodeoxycholic acid (CDCA) than the normal healthy pregnant women.

Pregnant women with asymptomatic hypercholanaemia of pregnancy had elevated conjugated dihydroxy serum bile acids than patients with normal serum bile acids.

This study concluded that there is a significant difference in the profile of serum bile acids between patients of obstetric cholestasis and normal pregnancies. There is a shift towards hydrophobic bile acid compositions in patients with obstetric cholestasis.

Egan et al and colleagues from Anu research centre, Department of OBGYN, Cork University Maternity hospital, Cork, Ireland, did a study to establish reference level for serum bile acids in pregnancy in all trimesters in healthy women. It was a cross sectional study. Sample size was 219.[23]

The values of serum bile acids were between 0.3 – 9.8 μmol/L in 216 women. There was no significant change in these levels all over pregnancy. To conclude, serum bile acid levels are constant and consistent throughout pregnancy and they are not elevated. Variation in the levels, if present, are very minimal.

Pascual MJ et al and colleagues conducted a study from the University of Salamanca, Spain, to determine the relationship between asymptomatic hypercholanaemia of pregnancy and the metabolites of progesterone.[24]

Sample size – 411 healthy pregnant women. Serum bile acids were analysed by enzymatic techniques and serum progesterones were analysed by ELISA technique. This study concludes that the serum bile acid pattern in both the obstetric cholestasis patients and AHP patients are the same. but the total serum progesterone levels were low and the levels of progesterone metabolites were high in patients with obstetric cholestasis.

Brites D et al, Rodriques CM et al from Pharmacy department, University of Lisbon, Portugal, conducted a study which compared 20 healthy women who are non pregnant and 77 women who are pregnant in the third trimester of pregnancy. Out of 77 pregnant women, 39 women suffered from obstetric cholestasis. Liver function tests including serum bile acids (both conjugated and unconjugated forms) were measured by normal laboratory techniques.[25]

Conclusion:

For the early diagnosis of obstetric cholestasis, the accurate and valid markers whose efficacy was 100% were,

1. Serum total bile acid concentration > 11.0 μmol/L.
2. Cholic/chenodeoxycholic acid >1.5.
3. Percentage of cholic acid >42%.
4. Glycine/taurine< 1.0.
5. Serum concentration of glycocholic acid > 2 μmol/L.

Ambros – Rudolph CM et al and colleagues from the Department of Dermatology, Medical University of Graz,Austria. It is a retrospective study, sample size – 13.These 13 cases of obstetric cholestasis represented 6% of all pregnancy associated dermatologic conditions. Secondary skin lesions like excoriations were present in 85% of the cases. All patients had

elevated serum bile acids and the level of serum bile acids were directly proportional to the adverse fetal outcomes. Preterm delivery rate was 100% in those patients not treated with UDCA whereas it was only 30% in those treated with UDCA.[26]

MATERIALS AND METHODS

SELECTION OF CASES:

INCLUSION CRITERIA:

The antenatal women in late second trimester and third trimester (24 – 40 weeks of gestational age) attending antenatal clinic, Kilpauk Medical College Hospital, Chennai, with complaints of pruritus and who satisfy exclusion criteria are included in the study. The period of study is between July 2010 and August 2012, for a period of 2 years.

EXCLUSION CRITERIA

1. Positive serology for hepatitis A,B,C.
2. Previous history of gall bladder disease.
3. Sonographic evidence of gall bladder disease.
4. Hypertension complicating pregnancy.
5. Liver function did not normalise within two weeks after delivery.
6. Autoimmune diseases like primary biliary cirrhosis, autoimmune chronic active hepatitis.

METHODOLOGY

- An interview was conducted using a questionnaire.
- Around 75 patients satisfying above criteria were chosen.
- LFT including Serum bilirubin, SGOT, SGPT, SAP, GGT was done. Patients were followed up with LFT and it was repeated at an interval of 2 weeks.
- LFT is repeated at 2 weeks after delivery.
- All patients were given Urso Deoxy Cholic Acid (UDCA) 8mg/kg/day in two divided doses.
- Time taken for onset of relief of pruritus was observed.
- Review of obstetric notes was done for Gestational age, Meconium staining of liquor, Mode of delivery, APGAR score, NICU admission, Birth weight.

SAMPLE SIZE

The sample size was calculated using the formula,

$$n = \frac{\mathrm{Z}\,2 \ * \ \mathrm{P}\,(1 - \mathrm{P})}{\mathrm{d}2}$$

Z - Constant (1.96).

P - Prevalence (0.05).

d - Desired precision (0.05).

By using this formula, *n* comes to 72 and the sample size for my study is 75.

RESULTS AND ANALYSIS

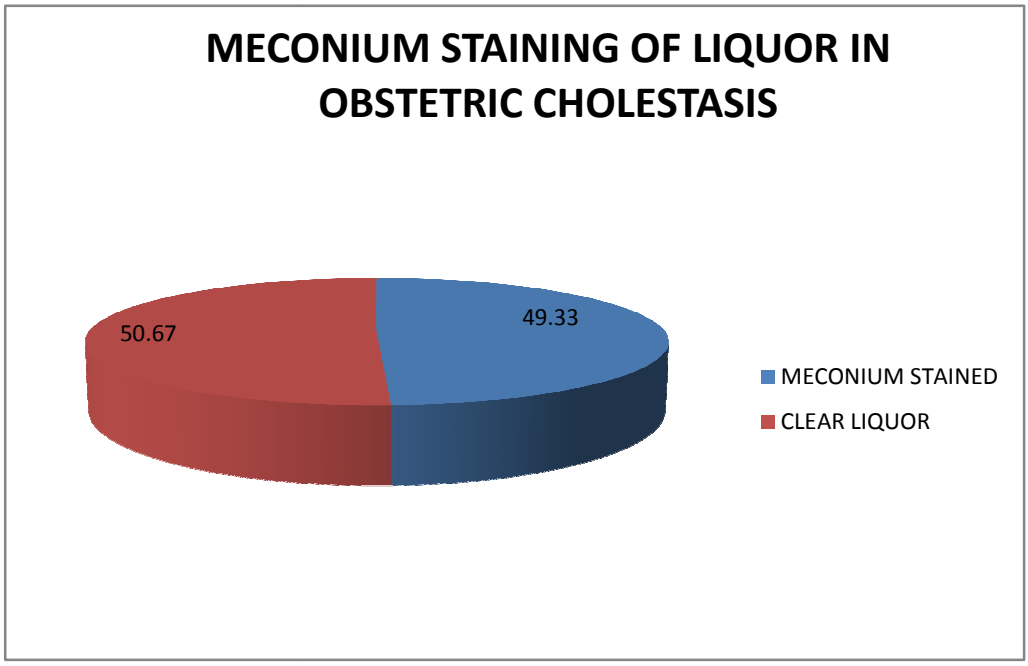
Results were analysed with computer statistical analysis system. Data's were compared using chi square test. Results were also analysed using proportion analysis by OPEN EPI software.

INCIDENCE OF OBSTETRIC CHOLESTASIS:

1000 patients were screened and 75 were diagnosed as having obstetric cholestasis, the incidence being **7.5%.**

OBSTETRIC CHOLESTASIS AND MECONIUM STAINING OF LIQUOR

Out of 75 patients with obstetric cholestasis, 37 patients **(49.7%)** were found to have meconium staining of liquor.



95% Confidence Limits for Proportion 37/75 Proportion: 49.33.

Fisher's Exact 37.58 %(lower) 61.14%(upper).

AGE GROUP AND MECONIUM STAINING OF LIQUOR

Out of 37 patients with meconium staining of liquor,17 patients (45.9%) belonged to age group of 21 – 24 years.

TABLE 1 :

			Meconium staining of liquor		
			NO	YES	Total
Agegroup	18-20	Count	4	4	8
		% within Meconium staining of liquor	10.5%	10.8%	10.7%
		% of Total	5.3%	5.3%	10.7%
	21-24	Count	18	17	35
		% within Meconium staining of liquor	47.4%	45.9%	46.7%
		% of Total	24.0%	22.7%	46.7%
	25-29	Count	14	14	28
		% within Meconium staining of liquor	36.8%	37.8%	37.3%
		% of Total	18.7%	18.7%	37.3%
	30-35	Count	2	2	4
		% within Meconium staining of liquor	5.3%	5.4%	5.3%
		% of Total	2.7%	2.7%	5.3%
	Total	Count	38	37	75
		% within Meconium staining of liquor	100.0%	100.0%	100.0%
		% of Total	50.7%	49.3%	100.0%

Mean age of patients with meconium staining of liquor is 23.86 yrs.

Mean age of patients with normal liquor is 23.95 yrs.

Group Statistics

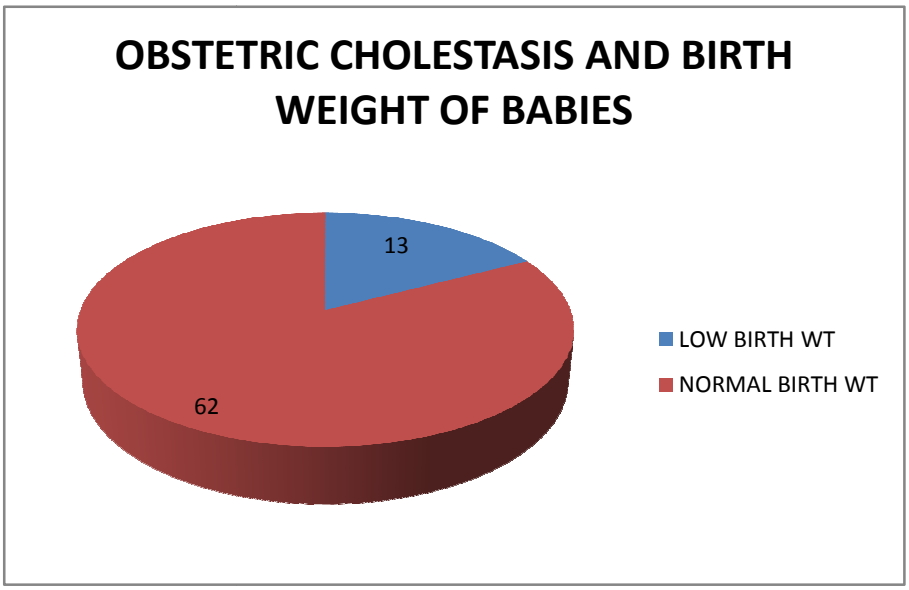
TABLE 2 :

Meconium staining of liquor		**N**	**Mean**	**Std. Deviation**	**Std. Error Mean**
	Yes	37	23.86	3.250	.534
	No	38	23.95	3.676	.596

P = 0.918 not significant.

OBSTETRIC CHOLESTASIS AND BIRTH WEIGHT OF BABIES

Out of 75 patients diagnosed to be having obstetric cholestasis,13 patients (17.3%) were found to have low birth weight babies.



95% Confidence Limits for Proportion 13/75 Proportion 17.33.

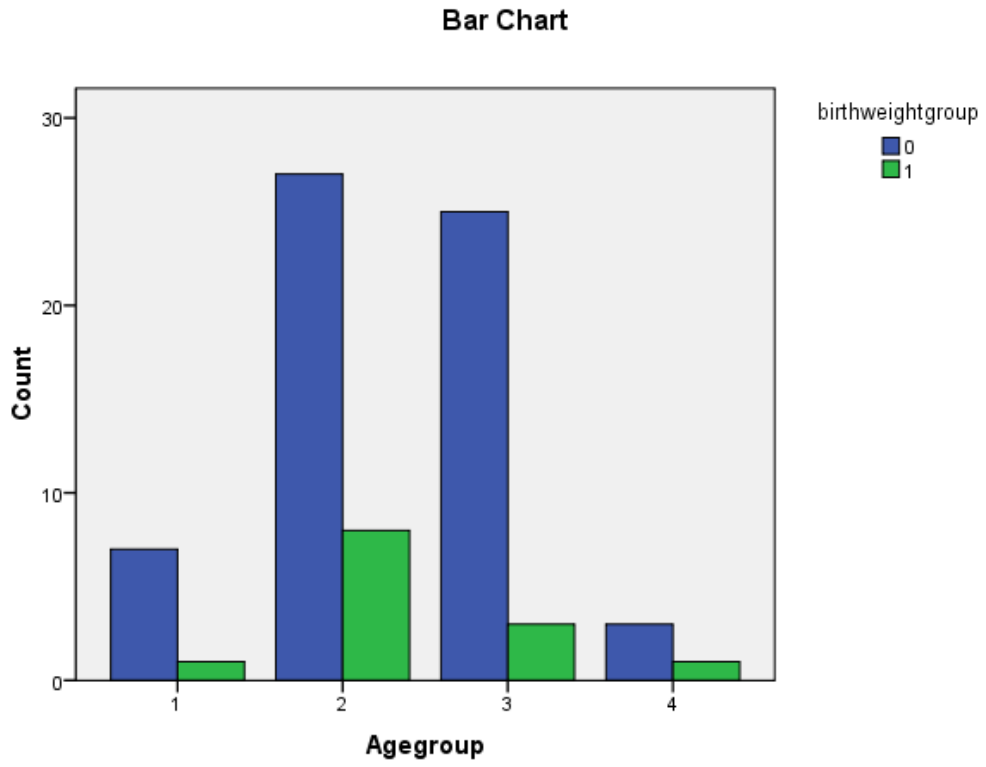
	Lower CL	Proportion (Percent)	UpperCL
Fisher's Exact	9.565%	17.33%	27.81%

AGE GROUP AND LOW BIRTH WEIGHT

Out of 13 patients who were found to have low birth weight babies,8 patients.(61.5%)belonged to age group of 21-24 yrs.

TABLE 3 :

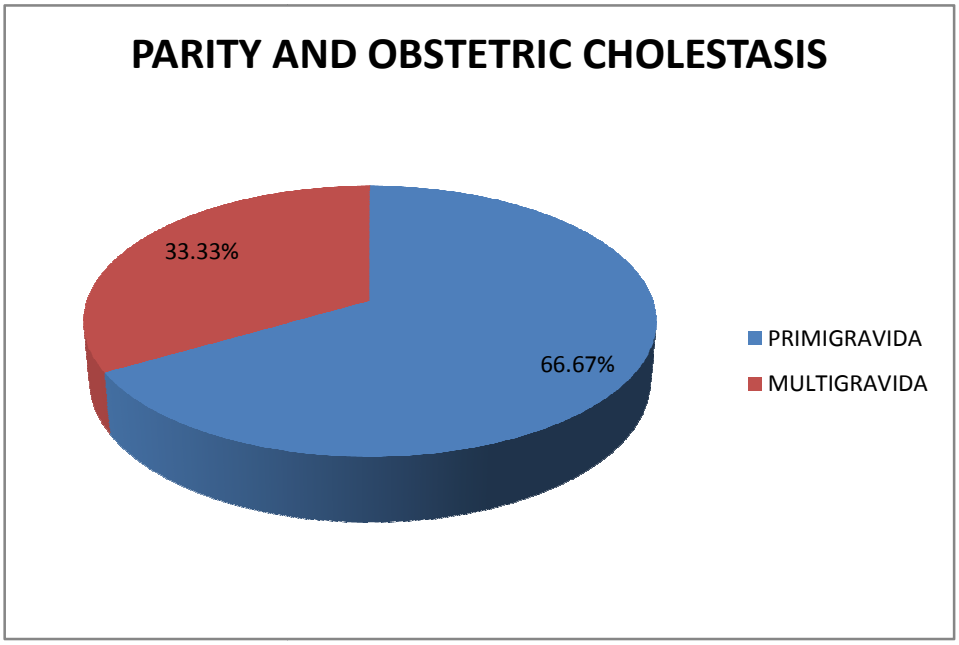
			Birth weight group		
			< 2.5 kg	>_2.5 kg	Total
Agegroup	18-20y	Count	7	1	8
		% within birth weight group	11.3%	7.7%	10.7%
		% of Total	9.3%	1.3%	10.7%
	21-24y	Count	27	8	35
		% within birth weight group	43.5%	61.5%	46.7%
		% of Total	36.0%	10.7%	46.7%
	25-29y	Count	25	3	28
		% within birth weight group	40.3%	23.1%	37.3%
		% of Total	33.3%	4.0%	37.3%
	30-35y	Count	3	1	4
		% within birth weight group	4.8%	7.7%	5.3%
		% of Total	4.0%	1.3%	5.3%
	Total	Count	62	13	75
		% within birth weight group	100.0%	100.0%	100.0%
		% of Total	82.7%	17.3%	100.0%


Bar Chart
birthweightgroup
0
1
Count
30
20
10
0
1
2
3
4
Agegroup

OBSTETRIC CHOLESTASIS AND PARITY

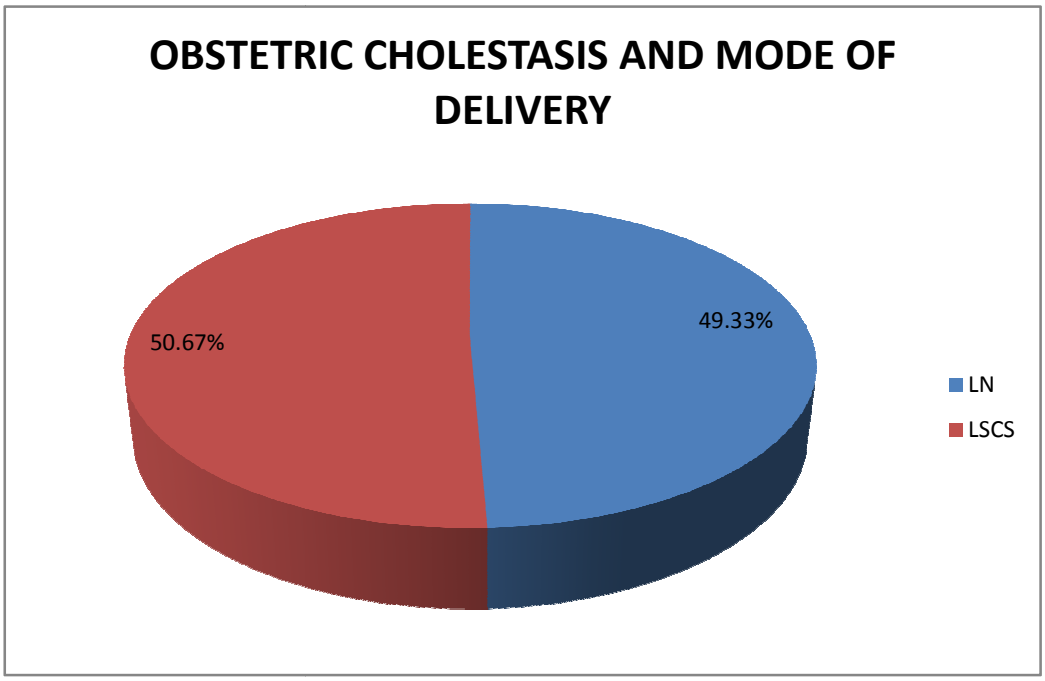
Out of 75 patients with obstetric cholestasis,50 patients (66.67%) were primigravida.

Obstetric cholestasis is more common in primigravida than in multigravidas.



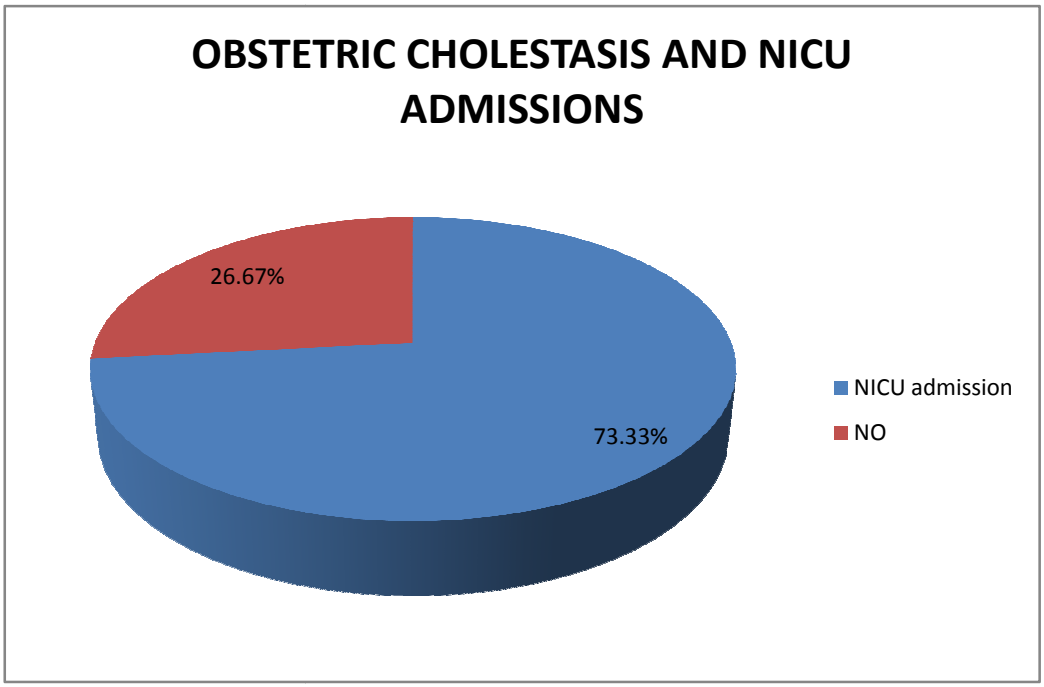
OBSTETRIC CHOLESTASIS AND MODE OF DELIVERY

Out of 75 patients with obstetric cholestasis,38 patients (50.67%) were delivered by LSCS.



OBSTETRIC CHOLESTASIS AND NICU ADMISSION

Babies of 55 patients with obstetric cholestasis (73.33%) were admitted in NICU.

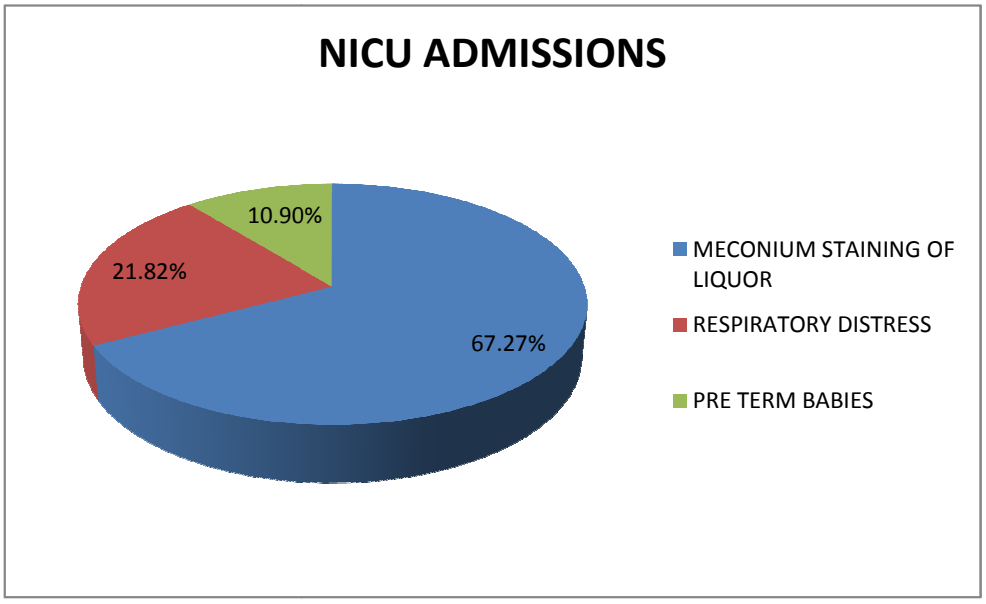


REASONS FOR NICU ADMISSION

The reasons for NICU admissions were Meconium staining of liquor, Respiratory distress and Preterm baby.

TABLE 4 :

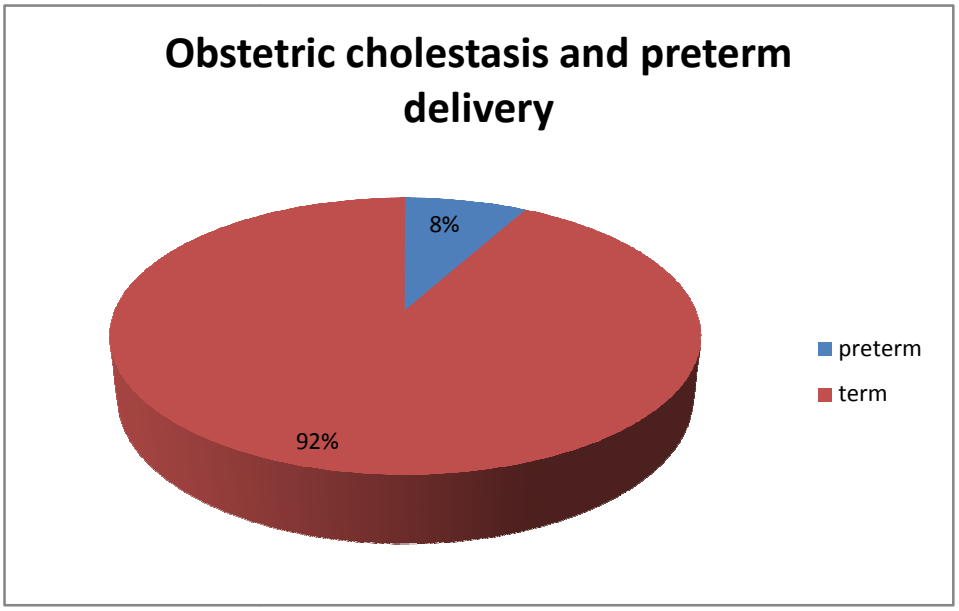
NICU ADMISSIONS	55	100%
MECONIUM STAINED LIQUOR	37	67.27%
RESPIRATORY DISTRESS	12	21.82%
PRETERM BABY	6	10.90%



67.27% of NICU admissions were due to Meconium staining of liquor. The remaining were due to respiratory distress and preterm deliveries.

OBSTETRIC CHOLESTASIS AND PRETERM DELIVERY

Out of 75 patients with obstetric cholestasis, 6 patients (8%) had preterm deliveries.



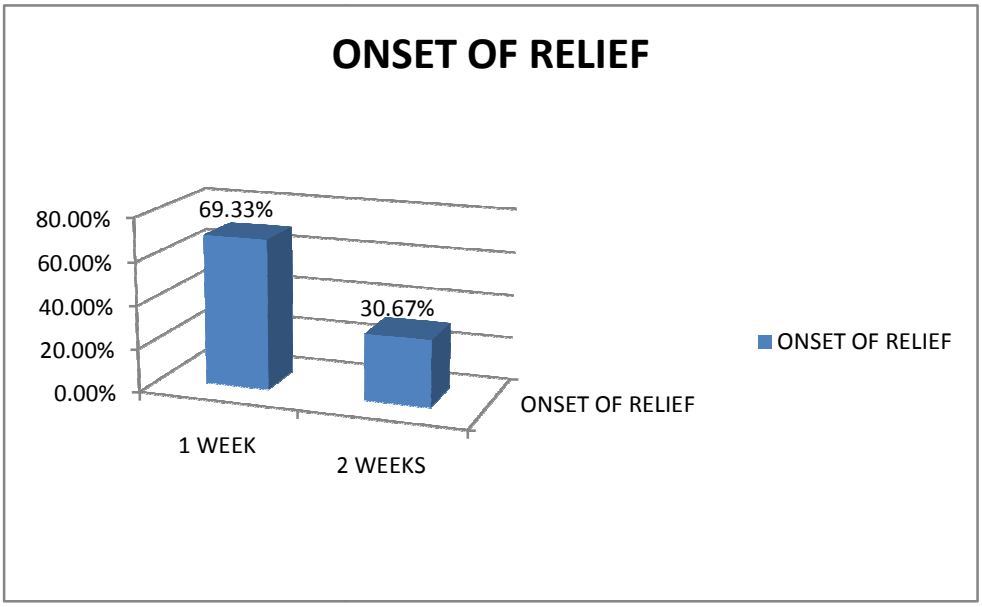
MEAN GESTATIONAL AGE AT DIAGNOSIS OF OBSTETRICCHOLESTASIS.

Mean GA at diagnosis of obstetric cholestasis was 32 weeks. Obstetric cholestasis was diagnosed as earlier as 25 weeks.

ONSET OF RELIEF WITH UDCA

52 patients (69.33%) had onset of relief in 1 week.

23 patients (30.67%) had onset of relief in 2 weeks.



OBSTETRIC CHOLESTASIS AND SERUM BILIRUBIN

Mean serum bilirubin level in patients with obstetric cholestasis is 0.74 mg/dl.

Highest serum bilirubin value – 0.9 mg/dl.

Lowest serum bilirubin value – 0.6 mg/dl.

ASSOCIATION BETWEEN SERUM BILIRUBIN AND MECONIUM STAINING OF LIQUOR

TABLE 5 :

Meconium Staining of Liquor		N	Mean	Std. Deviation	Std. Error Mean
Serum bilirubin mean	Yes	36	.74	.080	.013
	No	37	.74	.073	.012

P = 0.809 not significant.

OBSTETRIC CHOLESTASIS AND SGOT

Mean SGOT level in patients with obstetric cholestasis – 60.5 IU/L.

Highest SGOT value – 146 IU/L.

Lowest SGOT value – 22 IU/L.

ASSOCIATION BETWEEN SGOT LEVELS AND MECONIUM STAINING OF LIQUOR

TABLE 6 :

Meconium staining of liquor		N	Mean	Std. Deviation	Std. Error Mean
SGOT mean	1	37	65.65	32.466	5.337
	0	38	55.42	18.686	3.031

p = 0.098 not significant.

OBSTETRIC CHOLESTASIS AND SGPT

Mean SGPT level in patients with obstetric cholestasis – 57.8 IU/L.

Highest SGPT value – 124 IU/L.

Lowest SGPT value – 42 IU/L.

ASSOCIATION BETWEEN SGPT LEVELS AND MECONIUM STAINING OF LIQUOR

TABLE 7 :

Meconium staining of liquor		N	Mean	Std. Deviation	Std. Error Mean
SGPT mean	1	37	62.54	22.665	3.726
	0	38	53.00	13.164	2.136

p = 0.028 significant.

OBSTETRIC CHOLESTASIS AND GGT

GGT is raised only in 33.33% of patients with obstetric cholestasis.

Mean GGT level in patients with obstetric cholestasis is 36.4 IU/L.

Highest GGT value – 66 IU/L.

ASSOCIATION BETWEEN GGT LEVELS AND MECONIUM STAINING OF LIQUOR

TABLE 8 :

Meconium staining of liquor		N	Mean	Std. Deviation	Std. Error Mean
GGT mean	1	37	37.22	17.003	2.795
	0	38	35.58	14.899	2.417

p = 0.658 not significant.

OBSTETRIC CHOLESTASIS AND SAP

Mean SAP level in patients with obstetric cholestasis – 448.6 IU/L.

Highest SAP value – 786 IU/L.

Lowest SAP value – 380 IU/L.

ASSOCIATION BETWEEN SERUM SAP LEVELS AND MECONIUM STAINING OF LIQUOR

TABLE 9 :

Meconium staining of liquor		N	Mean	Std. Deviation	Std. Error Mean
SAP mean	Yes	37	469.35	75.535	12.418
	No	38	427.82	70.455	11.429

p = 0.016 significant

ASSOCIATION BETWEEN MECONIUM STAINING OF LIQUOR AND MODE OF DELIVERY

Out of 37 babies with meconium staining of liquor,24 (64.9%) were deliveredbylabournaturale and 13 (35.1%) were delivered by LSCS.

TABLE 10 :

		Meconium Staining of Liquor			
			No	**Yes**	**Total**
Mode of Delivery	LN	Count	13	24	37
		% within Meconium staining of liquor	34.2%	64.9%	49.3%
		% of Total	17.3%	32.0%	49.3%
	LSCS	Count	25	13	38
		% within Meconium staining of liquor	65.8%	35.1%	50.7%
		% of Total	33.3%	17.3%	50.7%
	Total	Count	38	37	75
		% within Meconium staining of liquor	100.0%	100.0%	100.0%
		% of Total	50.7%	49.3%	100.0%

Chi square – 7.048

p value = 0.08 significant.


Bar Chart
Meconium staining of liquor
0
1
Count
25
20
15
10
5
0
LN
LSCS
Mode of delivery

MODE OF DELIVERY AND NICU ADMISSION

Out of 55 babies admitted in NICU,30 babies (54.5%) were delivered by labournaturale and 25 babies (45.5%) were delivered by LSCS.

TABLE 11 :

			NICU Admission		
			0	1	Total
Mode of delivery	LN	Count	7	30	37
		% within NICU abdmission	35.0%	54.5%	49.3%
		% of Total	9.3%	40.0%	49.3%
	LSCS	Count	13	25	38
		% within NICU abdmission	65.0%	45.5%	50.7%
		% of Total	17.3%	33.3%	50.7%
	Total	Count	20	55	75
		% within NICU abdmission	100.0%	100.0%	100.0%
		% of Total	26.7%	73.3%	100.0%

Chi square – 2.242. p = 0.134 not significant

DISCUSSION

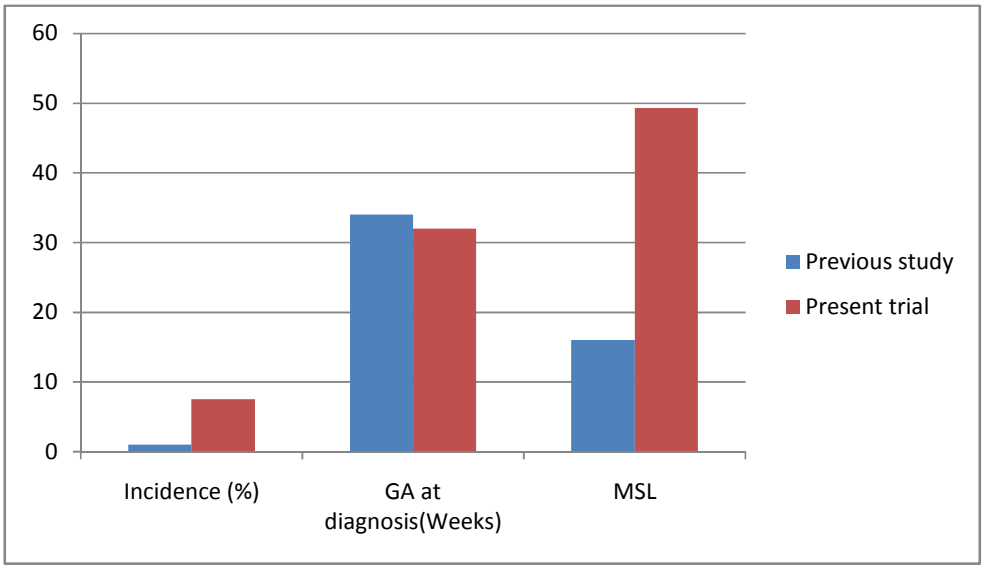
Obstetric cholestasis is a disease which is highly under reported. It was once considered to be a benign condition but it is not so. Its significance has been highlighted only recently due to associated maternal and perinatal morbidity and mortality.

Meconium staining of liquor and preterm labours many of the times go unrecognised as we do not consider about obstetric cholestasis as a cause. The aim of my study was to find the incidence of obstetric cholestasis, study the course of pregnancy and the pregnancy outcome in patients with obstetric cholestasis.

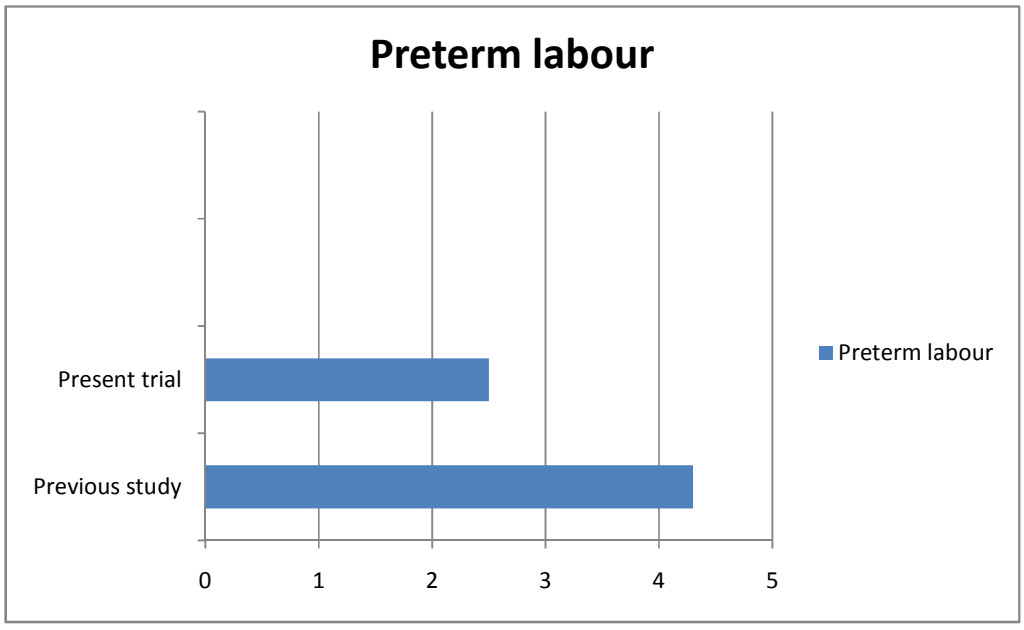
There are only few studies regarding obstetric cholestasis and its pregnancy outcome.

The study conducted by Roncaglia et al and Arreghini et al from Italy concluded that the incidence of obstetric cholestasis was 1%.The mean gestational age at diagnosis was at 34 weeks. The rate of meconium staining of liquor was 16%. In their study, there was no significant correlation

between obstetric cholestasis and meconium staining of liquor and this is reflected in my study too.



Wong LF et al, Shallow H et al,O'Connel MP et al conducted a study on the outcome of IHCP from Ireland.The percentage of preterm labour was 18% in their study while it was 8% in my study.



The percentage of meconium staining of liquor in my study was 49.33% which was very high when compared to all the other studies. The mean gestational age at diagnosis was 32 weeks in my study and this goes along all the other studies. The rate of preterm delivery is very low in my study when compared to aforementioned studies.

Having proved the association of Obstetric Cholestasis with adverse fetal outcomes, it becomes necessary to enquire about pruritus (which they may not disclose by themselves) in all pregnant women attending AN OP and if the answer is yes, carry on with other investigations necessary to prove the diagnosis. Careful follow up of patients with good antepartum, intrapartum fetal monitoring with appropriate interventions may reduce fetal morbidity and mortality.

SUMMARY

75 antenatal patients out of 1000 screened, who fulfilled the inclusion criteriawere included in the study and followed up till 2 weeks after delivery.

- 75 patients out of 1000 screened were found to be having obstetric Cholestasis (7.5%).
- Mean age of patients with obstetric cholestasis was 23.5 yrs.
- Mean birth weight of babies of mothers with obstetric cholestasis was 2.6 Kg.
- The incidence of meconium staining of liquor in patients with obstetric Cholestasis was 49.33%.
- The incidence of low birth weight in patients with obstetric cholestasis was 17.3%.
- 50.67 % of obstetric cholestasis patients were delivered by LSCS and 49.33 % were delivered by labour natural.
- Out of 75 patients with obstetric cholestasis,50 (66.67%) were primigravida.
- Babies of 55 patients with obstetric cholestasis (73.33%) were admitted in NICU.
- Meconium staining of liquor contributed to 67.27% of NICU admissions.

- The mean gestational age at diagnosis of obstetric cholestasis was 32 weeks
- All the patients with obstetric cholestasis were given UDCA and all of them were completely relieved of their symptoms.23 patients (30.6%) had onset of relief in 2 weeks and 52 patients (69.33%) had onset of relief in a week.
- Mean serum bilirubin level in obstetric cholestasis was 0.74 mg/dl.
- Highest serum bilirubin value – 0.9 mg/dl.
- Lowest serum bilirubin value – 0.6 mg/dl.
- There is no significant correlation between serum bilirubin levels and meconium staining of liquor.
- Mean SGOT levels in patients with obstetric cholestasis is 60.5 IU/L.
- Highest SGOT value – 146 IU/L.
- Lowest SGOT value – 22 IU/L.
- There is no significant correlation between SGOT levels and meconium staining of liquor.
- Mean SGPT levels in patients with obstetric cholestasis is 57.8 IU/L.
- Highest SGPT value – 124 IU/L.
- Lowest SGPT value – 42 IU/L.
- There exists significant correlation between SGPT levels and meconium staining of liquor.

- ❖ GGT is raised only in 33.33% of patients with obstetric cholestasis.
- ❖ Mean GGT levels in patients with obstetric cholestasis is 36.4 IU/L.
- ❖ Highest GGT value – 66 IU/L.
- ❖ Lowest GGT value – 18 IU/L.
- ❖ There is no significant correlation between GGT levels and meconium staining of liquor.
- ❖ Mean SAP levels in patients with obstetric cholestasis is 448.6 IU/L.
- ❖ Highest SAP value – 786 IU/L.
- ❖ Lowest SAP value – 380 IU/L.
- ❖ There exists a significant correlation between SAP levels and meconium staining of liquor.

CONCLUSION

- The incidence of obstetric cholestasis in the antenatal OP population of Kilpauk Medical College, a tertiary care center is 7.5%.
- Obstetric cholestasis is more common in primigravida than in multigravida.
- There is a significant association between obstetric cholestasis and meconium staining of liquor and NICU admissions.
- Obstetric cholestasis is more common in the age group of 21-24 yrs.
- The mean gestational age at diagnosis of obstetric cholestasis is 32weeks.
- There exists a significant correlation between SGPT levels, SAP levels and meconium staining of liquor.
- GGT and SGOT levels do not have significant association with meconium staining of liquor.
- Serum bilirubin levels were normal in all cases of obstetric cholestasis.
- UDCA provided symptomatic relief in all the patients with obstetric cholestasis.
- The incidence of preterm deliveries in obstetric cholestasis is 8%.
- There were no cases of prolonged pregnancy and intrauterine growth retardation in patients with obstetric cholestasis.
- The mean birth weight of babies with obstetric cholestasis –2.6 kg.
- Mode of delivery does not have significant correlation with obstetric cholestasis.

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PROFORMA

NAME :

AGE :

ADDRESS :

OBSTETRIC SCORE :

MENSTRUAL HISTORY :

LMP :

EDD :

GESTATIONAL AGE :

CHIEF COMPLAINTS :

PRESENT HISTORY :

1. Jaundice
2. Malaise
3. Insomnia
4. Skin rash
5. Anorexia
6. Dark urine
7. Pale stools
8. PIH

PAST HISTORY :

1. Jaundice
2. Gall stones
3. Similar complaints in previous pregnancy
4. h/o OCPs intake
5. hypertension

FAMILY HISTORY :

H/O obstetric cholestasis in family members

INVESTIGATIONS :

1. anti HAV
2. anti HCV
3. anti HEV
4. HBsAg
5. Sr bilirubin
6. SGOT
7. SGPT
8. SAP
9. GGT

UDCA :

DELIVERY DETAILS :

1. Date & Time :
2. Mode of delivery :
3. Indication :
4. PROM :
5. Preterm labour :
6. Liquor :
7. Birth weight :
8. APGAR :
9. NICU admission :
10. Post partum haemorrhage :

LFT AFTER 2 WEEKS :

MASTER CHART

Sl. No.	Name	Age	Age group	Obstetric score	GA at diagnosis (weeks)	Serum bilirubin mean (mg/dl)	serum bilirubin final (mg/dl)	SGOT mean (IU/L)	SGOT final (IU/L)	SGPT mean (IU/L)	SGPT final (IU/L)	GGT mean (IU/L)	GGT final (IU/L)	SAP mean (IU/L)	SAP Final (IU/L)	Mode of delivery	Meconium staining of liquor	UDCA	Relief	Onset of relief (weeks)	Birth weight (Kg)	NICU abd mission	IUGR	Prolonged pregnancy
1	Nithya	18	1	1	34	o.7	0.7	42	38	48	36	45	18	380	126	LN	no	yes	yes	1	2.4	yes	no	no
2	Sathya	18	1	1	36	o.7	0.8	40	32	56	41	57	22	410	66	LN	yes	yes	yes	2	2.5	yes	no	no
3	Monica	18	1	1	34	0.6	0.8	42	38	46	38	54	26	432	82	LN	yes	yes	yes	1	2.5	yes	no	no
4	Shagidha	19	1	1	28	0.7	0.8	22	42	44	40	64	26	408	110	LN	yes	yes	yes	2	3	yes	no	no
5	Priya	20	1	1	32	0.7	0.8	54	36	48	34	45	24	412	78	LSCS	no	yes	yes	1	2.8	no	no	no
6	Shobana	20	1	1	34	0.8	0.7	46	34	52	32	28	22	382	92	LN	no	yes	yes	1	2.5	yes	no	no
7	Divya	20	1	2	34	0.7	0.8	44	36	54	34	31	27	440	112	LN	no	yes	yes	1	2.8	no	no	no
8	Swapna	20	1	1	32	0.7	0.8	58	34	52	30	62	30	442	68	LN	yes	yes	yes	1	2.7	yes	no	no
9	Gomathy	21	2	1	33	0.8	0.8	62	40	66	32	22	16	436	94	LN	yes	yes	yes	2	3.1	yes	no	no
10	Kousalya	21	2	2	28	0.6	0.7	24	34	42	30	28	18	424	124	LSCS	no	yes	yes	2	2.4	no	no	no
11	Suhasini	21	2	2	28	0.8	0.7	68	38	44	38	22	24	412	68	LSCS	no	yes	yes	1	2.5	yes	no	no
12	Monisha	21	2	2	30	0.8	0.8	48	38	46	34	71	26	416	84	LSCS	no	yes	yes	1	2.8	no	no	no
13	Shakira	21	2	1	33	0.7	0.8	64	38	46	40	32	22	396	86	LN	yes	yes	yes	1	3	yes	no	no
14	Kavitha	21	2	1	36	0.7	0.9	68	34	58	22	35	16	456	92	LSCS	no	yes	yes	1	2.8	no	no	no
15	Nagalaksh	21	2	1	34	0.8	0.9	64	32	52	38	21	24	398	124	LN	no	yes	yes	1	2.6	no	no	no
16	Nandhini	21	2	1	30	0.8	0.8	48	38	46	32	26	24	412	96	LN	no	yes	yes	2	2.8	yes	no	no
17	Radhika	21	2	1	32	0.8	0.8	48	32	44	34	58	22	418	78	LSCS	no	yes	yes	2	2.7	no	no	no
18	Janaki	21	2	1	34	0.6	0.7	64	34	48	32	24	20	422	68	LSCS	no	yes	yes	1	3.2	yes	no	no
19	Malini	21	2	1	32	0.8	0.7	62	32	50	34	22	26	456	92	LN	yes	yes	yes	1	2.7	yes	no	no
20	Amudhaval	21	2	1	28	0.7	0.8	24	34	44	30	26	24	386	84	LN	yes	yes	yes	2	2.6	yes	no	no
21	Mohana	21	2	1	32	0.6	0.8	66	36	46	32	22	22	424	68	LN	yes	yes	yes	1	2.3	yes	no	no
22	Stella	22	2	1	33	0.7	0.9	64	40	54	35	65	20	436	94	LSCS	yes	yes	yes	1	2.7	yes	no	no
23	Sathya	22	2	1	31	0.8	0.8	62	38	64	32	27	30	386	86	LSCS	no	yes	yes	1	2.7	no	no	no
24	Poongodi	22	2	1	36	0.8	0.7	64	36	46	35	24	11	392	125	LSCS	no	yes	yes	1	2.5	yes	no	no

25	Teenamary	22	2	1	30	0.7	0.7	52	34	54	32	64	16	384	130	LSCS	no	yes	yes	1	2.5	yes	no	no
26	Sindhu	22	2	2	32	0.8	0.8	48	32	56	40	26	18	412	98	LSCS	yes	yes	yes	1	2.5	yes	no	no
27	Nikitha	22	2	1	34	0.8	0.7	92	40	124	33	74	22	634	136	LSCS	yes	yes	yes	1	2.4	yes	no	no
28	Manju	22	2	1	35	0.9	0.7	48	32	48	28	66	24	526	148	LN	yes	yes	yes	1	2.7	yes	no	no
29	Kalaiarasi	22	2	1	32	0.7	0.7	52	38	50	30	34	26	424	126	LN	no	yes	yes	2	2.6	yes	no	no
30	Jamuna	22	2	1	36	0.8	0.8	86	32	74	30	22	15	542	99	LN	yes	yes	yes	1	2.3	yes	no	no
31	Jeevitha	22	2	2	30	0.7	0.7	52	36	48	30	24	16	522	86	LSCS	yes	yes	yes	1	2.7	yes	no	no
32	Gajalaksh	22	2	1	32	0.6	0.8	112	32	98	32	47	24	564	88	LN	yes	yes	yes	2	2.75	yes	no	no
33	SELVI	22	2	1	36	0.9	0.8	54	36	63	24	45	26	388	94	LSCS	no	yes	yes	1	2.5	yes	no	no
34	Indhumath	23	2	1	25	0.7	0.7	52	32	46	30	26	24	428	92	LSCS	no	yes	yes	1	2.2	yes	no	no
35	Saritha	23	2	2	27	0.8	0.8	24	40	42	32	18	18	396	94	LN	yes	yes	yes	2	2.4	yes	no	no
36	Vanishree	23	2	1	34	0.8	0.8	48	34	54	34	53	20	416	86	LSCS	yes	yes	yes	1	2.4	yes	no	no
37	Nalini	23	2	1	33	0.8	0.8	46	34	48	21	24	24	396	112	LSCS	no	yes	yes	1	2.7	yes	no	no
38	Sumathy	23	2	1	39	0.7	0.7	68	36	62	30	28	32	382	98	LN	no	yes	yes	1	2.8	no	no	no
39	Pattu	23	2	2	28	0.7	0.8	32	34	42	32	27	32	426	86	LN	yes	yes	yes	1	2.8	yes	no	no
40	Kalaiarasi	23	2	2	32	0.7	0.7	48	32	46	36	64	28	398	88	LSCS	no	yes	yes	1	2.8	yes	no	no
41	Devi	23	2	1	29	0.8	0.7	36	32	42	30	28	26	392	90	LN	yes	yes	yes	1	2.75	yes	no	no
42	Muthulaks	23	2	1	35	0.6	0.7	146	34	114	32	22	24	546	99	LN	no	yes	yes	1	3.2	no	no	no
43	Jumma	24	2	2	32	0.7	0.7	48	32	46	28	24	26	486	112	LN	yes	yes	yes	1	2.25	yes	no	no
44	Sridevi	25	3	2	31	0.9	0.8	44	34	48	30	46	22	446	134	LSCS	no	yes	yes	1	2.75	no	no	no
45	Anitha	25	3	1	34	0.8	0.7	58	38	52	36	31	20	426	89	LN	yes	yes	yes	1	2.3	yes	no	no
46	Jayanthi	25	3	2	26	0.8	0.8	44	38	42	34	36	24	389	93	LSCS	no	yes	yes	1	3	yes	no	no
47	Sandhya	25	3	1	32	0.7	0.8	46	34	52	26	47	26	468	94	LSCS	yes	yes	yes	1	2.75	yes	no	no
48	Jagadha	25	3	2	32	0.8	0.8	60	34	58	30	32	24	428	96	LSCS	no	yes	yes	1	2.8	yes	no	no
49	Ashwini	25	3	1	30	0.8	0.8	46	32	48	32	22	26	398	124	LN	no	yes	yes	2	2.8	yes	no	no
50	Kalaiselvi	25	3	1	34	0.7	0.8	92	32	86	48	27	22	786	126	LSCS	no	yes	yes	1	2.8	no	no	no
51	Saranya	26	3	1	36	0.7	0.7	58	34	50	28	53	24	428	122	LSCS	no	yes	yes	1	2.7	no	no	no
52	Menaka	26	3	1	34	0.8	0.8	46	34	48	34	21	20	388	114	LSCS	no	yes	yes	1	2.6	no	no	no
53	Paramesh	26	3	2	34	0.9	0.7	66	32	58	26	24	18	422	46	LSCS	yes	yes	yes	1	3.1	yes	no	no
54	Eswari	26	3	2	34	0.8	0.7	48	34	46	28	65	14	392	96	LN	yes	yes	yes	2	2.5	yes	no	no
55	Padmasree	26	3	1	34	0.7	0.8	50	34	52	22	25	24	462	86	LSCS	yes	yes	yes	2	2.8	yes	no	no
56	Bharathy	26	3	2	32	0.7	0.8	52	34	62	36	28	26	398	78	LSCS	no	yes	yes	2	2.3	yes	no	no

57	Rajalakshm	26	3	2	30	0.7	0.8	48	37	46	34	26	32	436	74	LSCS	yes	yes	yes	yes	2	3	yes	no	no
58	Shyamala	26	3	1	35	0.6	0.8	146	40	102	32	56	22	624	82	LN	yes	yes	yes	yes	2	2.75	yes	no	no
59	Saranya	26	3	1	35	0.7	0.7	64	38	66	36	24	20	346	84	LN	yes	yes	yes	yes	2	2.6	yes	no	no
60	Chitra	27	3	1	35	0.7	0.8	52	40	48	32	26	18	386	96	LSCS	no	yes	yes	yes	1	2.7	no	no	no
61	Loordhu	27	3	2	34	0.7	0.8	114	36	98	28	21	16	654	108	LSCS	yes	yes	yes	yes	1	3	yes	no	no
62	Bharathy	27	3	2	28	0.7	0.8	42	37	46	32	28	24	488	92	LSCS	yes	yes	yes	yes	1	2.5	yes	no	no
63	Esther	27	3	1	34	0.8	0.7	48	40	52	28	34	22	512	112	LN	yes	yes	yes	yes	2	2.5	yes	no	no
64	Saritha	27	3	1	29	0.7	0.8	44	40	51	30	32	20	546	104	LN	no	yes	yes	yes	1	2.75	no	no	no
65	Shalini	28	3	2	29	0.7	0.8	46	35	42	32	24	18	426	88	LSCS	no	yes	yes	yes	1	2.4	yes	no	no
66	Rajini	28	3	1	32	0.8	0.8	126	34	98	24	45	14	544	92	LN	yes	yes	yes	yes	1	2.6	yes	no	no
67	Eswari	28	3	2	34	0.7	0.8	52	32	50	26	24	16	436	106	LSCS	no	yes	yes	yes	1	2.6	no	no	no
68	Sajitha	29	3	1	34	0.7	0.7	54	35	48	28	31	22	386	68	LN	no	yes	yes	yes	2	2.75	no	no	no
69	Banumathy	29	3	2	38	0.8	0.7	60	34	62	30	28	20	456	86	LSCS	no	yes	yes	yes	2	2.7	no	no	no
70	Meenakum	29	3	1	32	0.7	0.8	143	32	76	32	28	24	436	98	LN	yes	yes	yes	yes	1	2.75	yes	no	no
71	Usha	29	3	2	32	0.7	0.8	88	34	88	24	46	22	568	86	LSCS	yes	yes	yes	yes	2	2.8	yes	no	no
72	Rajeshwari	30	4	2	32	0.9	0.7	96	35	106	22	20	18	482	76	LSCS	yes	yes	yes	yes	2	2.7	yes	no	no
73	Devi	30	4	1	31	0.7	0.8	116	34	98	27	22	20	564	84	LN	yes	yes	yes	yes	1	2.2	yes	no	no
74	Shanthi	33	4	2	28	0.7	0.8	44	35	50	32	66	24	436	92	LN	no	yes	yes	yes	1	2.7	no	no	no
75	Hemalatha	35	4	1	30	0.8	0.7	50	34	46	32	64	14	428	104	LN	no	yes	yes	yes	2	2.8	yes	no	no

Ethical Committee Certificate

ETHICAL COMMITTEE
GOVT. KILPAUK MEDICAL COLLEGE, KILPAUK,
CHENNAI- 10.
Venue: PANAGAL HALL, KMC
Dt: 01.02.2011

CHAIRPERSON
Prof. Dr.V.KANAGASABAI, MD.,
Dean
Govt. Kilpauk Medical College, Chennai-10
Sub: Ethical Committee project work - approved – regarding.
Ref: Lr.No.3944/Audit/E1/09 Dt. 30.11.2010

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With above reference, the Institutional Ethical committee meeting for the following students was conducted at our Institution on 01.02.2011.

S.NO.	Name	Topic
1.	Dr.Navin Kumar, MS(Ortho), PG., Govt. Royapettah Hospital, Chennai.	1.To Identify a Safe Zone to approach proximal Humerus 2.To study Anatomical relations of Axillary nerve, its course & its Variations
2.	Dr.T.Satheesh Kumar, D.Ortho., PG., Govt. Royapettah Hospital, Chennai	Heriditary Multiple Exostosis
3.	Dr.J. Jeya Shambavi, MD(Pathology), PG., Govt. Kilpauk Medical College, Chennai-10	Clinicopathological Histomorphological and Immunohistochemical Study of Neuroendocrine Tumors of GIT
4.	Dr.L. R. Saranya. MD., (Paed.)PG., Govt. Kilpauk Medical College, Chennai-10	Cord Blood Zinc Level in Term-Small for Gestational Age Neonates
5.	Dr.A.Satheesh Kumar, MS(ENT), PG., Kilpauk Medical College, Chennai	Study on Cases of Chronic Suppurative Otitis Media in Tubo Tympanic Type Due to Sinusitis as Focal Sepsis
6.	R.Prathiban,(Msc.,Physiology), PG., Student, The TN. Dr.MGR Medical University,Chennai-32	Prevalence of Cardiac Dysautonomia in Type I Diabetes mellitus
7.	B. Manikandan, (Msc., Physiology), PG., Student, The TN Dr.M.G.R. Medical University, Chennai-32.	A Comparative Study of Left Ventricular Structure and Function in Obese and Non Obese Subjects
8.	G. Selvakumar, (MSc., Physiology), PG., Student, The TN Dr.M.G.R. Medical University, Chennai-32.	A Study of the Intraocular Pressure In Patients with Diabetic Normotensive, Diabetic Hypertensive and Normal Subjects

9.	R. Ragulji, (Msc.,Physiology), PG., The TN Dr.MGR Medical University, Chennai-32.	A Study of Pulmonary function in insulin dependent diabetes mellitus
10.	V.M. Jenila Veny,(MscPhysiology), PG. The TN Dr.MGR Medical University, Chennai-32	Cardiovascular Autonomic Dysfunction in Chronic Kidney Disease
11.	Dr.G. Lakshmi, MD(O&G), PG., Govt. Kilpauk Medical College,Chennai-10	A Study of Association of Thyroid Disorders in Abnormal Uterine Bleeding
12.	Dr.R. Harini, MD(O&G), PG., Kilpauk Medical College, Chennai	Single Dose Antibacterial treatment for Asymptomatic Bacteriuria in Pregnancy
13.	Dr.E.Geetha, MD(O&G), PG., Govt. Kilpauk Medical College, Chennai-10	A Study of the incidence course of Pregnancy and Pregnancy outcome in Obstetric Cholestasis and to evaluate the efficiency of UDCA in relieving the Symptoms and Improving the Perinatal outcome in these Patients
14.	Dr.S. Nithya, MD(O&G), PG., Govt. Kilpauk Medical College, Chennai-10	Prospective Study of Prevalence of diabetes Mellitus, Thyroid Dysfunction and Hyperprolactinemia in Recurrent Pregnancy loss
15.	Dr.Mohideen Fathima, MD(O&G), PG., Govt. Kilpauk Medical College, Chennai-10	A Study of evaluation of multi system changes in Gestational hypertension / severe pre-eclamptic/eclampasia patients
16.	Dr.M.Padma Priya, MD(O&G), PG., Kilpauk Medical College, Chennai	Dyslipidemia as a Predictor of PIH
17.	Mrs.G. Savitha, (Msc.,Medical Bio Chemistry), TN Dr.M.G.R.Medical University, Chennai-32.	Association of subclinical hypothyroidism in metabolic syndrome patients
18.	Dr.K. Bharadhwaj, MD(G.M.), PG., Kilpauk Medical College, Ch-10	A Study on Peripheral Vascular Disease in Type 2 Diabetes Mellitus
19.	Dr.B.Priya, MD(G.M.), PG	Study of Serum Bilirubin Concentration in Established Coronary Artery Disease
20.	Dr.R.Hema, MD(G.M.), PG.,	Study of Troponin I level in Supraventricular Tachycardia in Non Cad Patients
21.	Dr.P.Manoj Kumar, MD(G.M.), PG., Kilpauk Medical College, Ch-10	A Study on Pulmonary Functions in Type 2 Diabetes Mellitus
22.	Dr.M.Dhanasekar, MD(G.M.), PG.,	Prognostic Risk Stratification of Acute Coronary Syndrome – Role of Highly Sencitive – Reactive Protien
23.	Dr.N. Karthik, MD(G.M.), PG., Govt.Kilpauk Medical College, Chennai-10	A Study of Comparison of QT Dispersion in Acute Myocardial Infraction Between Early Reperfusion and Late Reperfusion Therapy

24.	Dr.H. Anuradha, MD(G.M.), PG., Kilpauk Medical College, Ch-10	A Study of Stress Hyperglycemia in Moderate Degree Burns
25	Dr. V. Nandakumar, MD(G.M.), PG.,	A Prospective Study of Clinical Profile of Emphysematous Pyelonephritis in Type Two Diabetes Mellitus
26.	Dr.S.Sasikumar, MS(G.S.), PG., Govt. Royapettah Hospital, Chennai	A Study of Unusual Presentations of Appendicitis.
27.	Dr.S.R.Padmanabhan, MS(GS), PG., Govt. Royapettah Hospital, Chennai	A Comparative Study Between Autologous Platelet Rich Plasma and Saline Dressing for Diabetic Ulcer
28.	Dr.C.Rose, Scientist-G and Head, Biotechnology, Central Leather Institute, Chennai.	Wound healing efficacy of the chitosan – containing collagenous biomaterial, on burn wound
29.	E.K. Lavanya,B.Tech, Biotechnology, PG., Prathyusha Institute of Technology and Management, Tiruvallur.	Isolation and Characterization of Bacterial Pathogens from Eye Infection

We are glad to inform you that at the Ethical Committee meeting, the documents were discussed and the above short term projects are Ethically approved.

4/2/11

CHAIRPERSON

. DEAN

Govt. Kilpauk Medical College,

Chennai-10.

To: The Individuals

சுய ஒப்புதல் படிவம்

ஆய்வு செய்யப்படும் தலைப்பு :

மகளிர் மற்றும் மகப்பேறு மருத்துவத்துறை :

கீழ்ப்பாக்கம் மருத்துவக்கல்லூரி :

பங்கு பெறுபவரின் பெயர் :

பங்கு பெருபவரின் வயது :

பங்கு பெருபவரின் எண் :

பங்கு பெறுபவர் இதனை (√) குறிக்கவும்.

- ❖ மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்கள் எனக்கு விளக்கப்பட்டது. என்னுடைய சந்தேகங்களை கேட்கவும் அதற்கான தகுந்த விளக்கற்களை கேட்க வாய்ப்பளிக்கப்பட்டடுள்ளது என அறிந்து கொண்டேன். ☐
- ❖ நான் இவ்வாய்வில் தன்னிச்சையாகத் தான் பங்கேற்கிறேன்.எந்த காரணத்தினாலோ எந்த சட்டசிக்களுக்கும் உட்படாமல் நான் இவ்வாய்வில் இருந்து விலகிக் கொள்ளலாம் என்றும் அறிந்து கொண்டேன். ☐
- ❖ இந்த ஆய்வு சம்பந்தமாகவோ அதை சார்ந்து மேலும் ஆய்வு மேற்கொள்ளும் போது இந்த ஆய்வில் பங்கு பெறும் மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளை பார்ப்பதற்கு என் அனுமதி தேவையில்லை என அறிந்து கொள்கிறோன். ☐
- ❖ இந்த ஆய்வின் மூலம் கிடைக்கும் தகவலையோ முடிவையோ பயன்படுத்திக் கொள்ள மறுக்கமாட்டோன். ☐
- ❖ இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக் கொள்கிறேன். இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உன்மையுடன் இருப்பேன் என்றும் உறுதியளிக்கிறேன். ☐
- ❖ இந்த ஆய்வில் ஒருமுறை 5 மி இரத்த பரிசோதனைக்காக எடுத்தக் கொள்ளப்படும் என்பதை அறிவேன்.

பங்கேற்பவரின் கையொப்பம்_____

இடம்_____ தேதி_____

பங்கேற்பவரின் பெயர் மற்றும் விலாசம்
சாட்சியாளரின் கையொப்பம்

இடம்_____ தேதி_____
சாட்சியாளரின் பெயர் மற்றும் விலாசம்

ஆய்வாளரின் கையொப்பம்
இடம்_____ தேதி_____
ஆய்வாளரின் பெயர்_____